

02-24-00

Customer No. 20350

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
(415) 576-0200

**ASSISTANT COMMISSIONER FOR PATENTS
BOX PATENT APPLICATION
Washington, D.C. 20231**



Attorney Docket No. 2307E-098010US

"Express Mail" Label No. EM530421283US

Date of Deposit: February 22, 2000

I hereby certify that this is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above, addressed to:

Sir:

Transmitted herewith for filing under 37 CFR 1.53(b) is the

- ☐ patent application of
- ☐ continuation patent application of
- ☐ divisional patent application of
- ☒ continuation-in-part patent application of

Assistant Commissioner for Patents
Washington, D.C. 20231

By: [Signature]

Inventor(s)/Applicant Identifier: Charles S. ZUKER, Jon Elliot ADLER, Nick RYBA and Ken MUELLER

For: T2R, A NOVEL FAMILY OF TASTE RECEPTORS

☒ This application claims priority from each of the following Application Nos./filing dates:

U.S. Application No. 09/393,634, filed September 10, 1999

the disclosure(s) of which is (are) incorporated by reference.

☐ Please amend this application by adding the following before the first sentence: "This application is a ☐ continuation ☐ continuation-in-part of and claims the benefit of U.S. Application No. _____, filed _____, the disclosure of which is incorporated by reference."

Enclosed are:

- ☒ 185 page(s) of specification
- ☒ 18 page(s) of claims
- ☒ 1 page of Abstract
- ☒ 45 sheet(s) of ☐ formal ☒ informal drawing(s).
- ☒ 1 Title page

☒ Assignments of the invention from Zuker and Mueller to The Regents of the University of California and from Adler and Ryba to The Government of the United States as Represented by the Secretary of the Department of Human Services is of record in the prior application no. 09/393,634

☐ A ☐ signed ☐ unsigned Declaration & Power of Attorney

☒ A ☐ signed ☒ unsigned Declaration.

☐ A Power of Attorney by Assignee with Certificate Under 37 CFR Section 3.73(b).

☐ A verified statement to establish small entity status under 37 CFR 1.9 and 37 CFR 1.27 ☐ is enclosed ☐ was filed in the prior application and small entity status is still proper and desired.

☐ A certified copy of a _____ application.

☐ Information Disclosure Statement under 37 CFR 1.97.

☐ A petition to extend time to respond in the parent application.

☐ Notification of change of ☐ power of attorney ☐ correspondence address filed in prior application.

In view of the unsigned declaration as filed with this application and pursuant to 37CFR 1.53(b), Applicant requests deferral of the filing fee until submission of the Missing Parts of this Application.

Do not charge the filing fee at this time.

Respectfully submitted,
TOWNSEND and TOWNSEND and CREW LLP

[Signature]

Peter J. Follette, Ph.D.

Reg No.: P-46,213

Attorneys for Applicant

Telephone:

(415) 576-0200

Facsimile:

(415) 576-0300

SF 1070045 v1



PATENT APPLICATION

T2R, A NOVEL FAMILY OF TASTE RECEPTORS

Inventor(s):

Charles S. Zuker, a citizen of the United States, residing at
4778 Thurston Place
San Diego, CA 92130

Jon Elliot Adler, a citizen of the United States, residing at
1730 P. St. NW
Washington, D.C. 20036

Nick Ryba, a citizen of the United Kingdom, residing at
9202 Lundigen Court
Bethesda, MD 20817

Ken Mueller, a citizen of the United States, residing at
9585 Genesee Ave., Apt H1, San Diego, CA 92121

Townsend and Townsend and Crew LLP
Two Embarcadero Center, 8th Floor
San Francisco, CA 94107
(415)576-0200

T2R, A NOVEL FAMILY OF TASTE RECEPTORS

5

CROSS-REFERENCES TO RELATED APPLICATIONS

This application claims priority to and is a continuation-in-part of USSN 09/393,634, filed September 10, 1999, which is herein incorporated by reference in its entirety.

10

STATEMENT AS TO FEDERALLY SPONSORED RESEARCH AND DEVELOPMENT

This invention was made with government support under Grant No. 5R01 DC03160, awarded by the National Institutes of Health. The government has certain rights in this invention.

15

FIELD OF THE INVENTION

The invention provides isolated nucleic acid and amino acid sequences of taste cell specific G-protein coupled receptors, antibodies to such receptors, methods of detecting such nucleic acids and receptors, and methods of screening for modulators of taste cell specific G-protein coupled receptors.

20

BACKGROUND OF THE INVENTION

Taste transduction is one of the most sophisticated forms of chemotransduction in animals (*see, e.g.*, Margolskee, *BioEssays* 15:645-650 (1993); Avenet & Lindemann, *J. Membrane Biol.* 112:1-8 (1989)). Gustatory signaling is found throughout the animal kingdom, from simple metazoans to the most complex of vertebrates; its main purpose is to provide a reliable signaling response to non-volatile ligands. Each of these modalities is though to be mediated by distinct signaling pathways mediated by receptors or channels, leading to receptor cell depolarization, generation of a receptor or action potential, and release of neurotransmitter at gustatory afferent neuron synapses (*see, e.g.*, Roper, *Ann. Rev. Neurosci.* 12:329-353 (1989)).

25

30

depolarization is hypothesized to result from H⁺ blockage of K⁺ channels (*see, e.g.,* Kinnamon *et al.*, *Proc. Nat'l Acad. Sci. USA* 85: 7023-7027 (1988)) or activation of pH-sensitive channels (*see, e.g.,* Gilbertson *et al.*, *J. Gen. Physiol.* 100:803-24 (1992)); salt transduction may be partly mediated by the entry of Na⁺ via amiloride-sensitive Na⁺ channels (*see, e.g.,* Heck *et al.*, *Science* 223:403-405 (1984); Brand *et al.*, *Brain Res.* 207-214 (1985); Avenet *et al.*, *Nature* 331: 351-354 (1988)).

Sweet, bitter, and umami transduction are believed to be mediated by G-protein-coupled receptor (GPCR) signaling pathways (*see, e.g.,* Striem *et al.*, *Biochem. J.* 260:121-126 (1989); Chaudhari *et al.*, *J. Neurosci.* 16:3817-3826 (1996); Wong *et al.*, *Nature* 381: 796-800 (1996)). Confusingly, there are almost as many models of signaling pathways for sweet and bitter transduction as there are effector enzymes for GPCR cascades (*e.g.,* G protein subunits, cGMP phosphodiesterase, phospholipase C, adenylate cyclase; *see, e.g.,* Kinnamon & Margolskee, *Curr. Opin. Neurobiol.* 6:506-513 (1996)). However, little is known about the specific membrane receptors involved in taste transduction, or many of the individual intracellular signaling molecules activated by the individual taste transduction pathways. Identification of such molecules is important given the numerous pharmacological and food industry applications for bitter antagonists, sweet agonists, and other modulators of taste.

One taste-cell specific G protein that has been identified is called Gustducin (McLaughlin *et al.*, *Nature* 357:563-569 (1992)). This protein is proposed to be involved in the detection of certain bitter and sweet tastes since gustducin knockout mice show decreased sensitivity to some sweet and bitter tastants (Wong *et al.*, *Nature* 381:796-800 (1996)), and because gustducin is expressed in a significant subset of cells from all types of taste papillae (McLaughlin *et al.*, *Nature* 357:563-569 (1992)). In addition, gustducin can be activated *in vitro* by stimulating taste membranes with bitter compounds, likely through the activation of bitter receptors (Ming *et al.*, *PNAS* 95:8933-8938 (1998)).

Recently, two novel GPCRs were identified and found to be specifically expressed in taste cells. While these receptor proteins, called TR1 and TR2, appear to be directly involved in taste reception (Hoon *et al.*, *Cell* 96:541-551 (1999)), they are only expressed in a fraction of mammalian taste receptor cells. For example, neither of the genes are extensively expressed in Gustducin-expressing cells. Thus, it is clear that additional taste-involved GPCRs remain to be discovered.

Genetic studies in mammals have identified numerous loci that are involved in the detection of taste. For example, psychophysical tasting studies have shown that humans can be categorized as tasters, non-tasters, and super-tasters for the bitter substance PROP (6-n-propylthiouracil), and that PROP tasting may be conferred by a dominant allele, with non-tasters having two recessive alleles and tasters having at least one dominant allele (see Bartoshuk *et al.*, *Physiol Behav* 56(6):1165-71; 58:203-204 (1994)). Recently, a locus involved in PROP tasting has been mapped to human interval 5p15 (Reed *et al.*, *Am. J. Hum. Genet.*, 64(5):1478-80 (1999)). The PROP tasting gene present at the 5p15 locus has yet to be described, however.

In addition, a number of genes involved in taste have been mapped in mice. For example, a cluster of genes involved in bitter-taste detection has been mapped to a region of chromosome 6 in mice (Lush *et al.*, *Genet Res.* 66:167-174 (1995)).

The identification and isolation of novel taste receptors and taste signaling molecules would allow for new methods of pharmacological and genetic modulation of taste transduction pathways. For example, the availability of receptor and channel molecules would permit the screening for high affinity agonists, antagonists, inverse agonists, and modulators of taste cell activity. Such taste modulating compounds would be useful in the pharmaceutical and food industries to customize taste. In addition, such taste cell specific molecules can serve as invaluable tools in the generation of taste topographic maps that elucidate the relationship between the taste cells of the tongue and taste sensory neurons leading to taste centers in the brain.

SUMMARY OF THE INVENTION

The present invention thus provides novel nucleic acids encoding a family of taste-cell specific G-protein coupled receptors. These nucleic acids and the polypeptides that they encode are referred to as the "T2R" family of G-protein coupled taste receptors. These receptors are also referred to as the "SF" family of G-protein coupled taste receptors. This novel family of GPCRs includes components of the taste transduction pathway. In particular, members of this family are involved in the detection of bitter tastes.

In one aspect, the present invention provides a method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of: (i) contacting a taste transduction G-protein coupled receptor polypeptide with the compound, the polypeptide comprising at least about 50% amino acid identity to a

sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171; and (ii) determining the functional effect of the compound upon the polypeptide.

In another aspect, the present invention provides a method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of: (i) contacting a taste transduction G-protein coupled receptor polypeptide with the compound, the polypeptide comprising greater than about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164; and (ii) determining the functional effect of the compound upon the polypeptide.

In another aspect, the present invention provides a method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of: (i) contacting a polypeptide comprising an extracellular domain or transmembrane region, or combination thereof, of a taste transduction G-protein coupled receptor with the compound, the extracellular domain or transmembrane region comprising greater than about 60% amino acid sequence identity to the extracellular domain or transmembrane

region of a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164; and (ii) determining the functional effect of the compound upon the extracellular domain or transmembrane region.

In one embodiment, the polypeptide has G-protein coupled receptor activity. In another embodiment, the functional effect is a chemical effect. In another embodiment, the functional effect is a physical effect. In another embodiment, the functional effect is determined by measuring binding of the compound to an extracellular domain of the polypeptide. In another embodiment, the functional effect is determined by measuring radiolabeled GTP binding to the polypeptide. In another embodiment, the polypeptide is recombinant. In another embodiment, the polypeptide comprises an extracellular domain or transmembrane region or a combination of an extracellular domain and transmembrane region that is covalently linked to a heterologous polypeptide, forming a chimeric polypeptide. In another embodiment, the polypeptide is linked to a solid phase, either covalently or non-covalently. In another embodiment, the polypeptide is from a rat, a mouse, or a human.

In another embodiment, the polypeptide is expressed in a cell or a cell membrane. In another embodiment, the cell is a eukaryotic cell. In another embodiment, the functional effect is measured by determining changes in the electrical activity of a cell expressing the polypeptide. In another embodiment, the functional effect of the compound upon the polypeptide is determined by measuring changes in intracellular cAMP, cGMP, IP3, or Ca^{2+} in a cell expressing the polypeptide. In another embodiment, a change in intracellular Ca^{2+} in the cell is detected by detecting FURA-2 dependent fluorescence in the cell. In another embodiment, the cell is a eukaryotic cell. In another embodiment, the cell is an HEK-293 cell. In another embodiment, the polypeptide is a fusion protein comprising at least about 20 consecutive N-terminal amino acids of a rhodopsin protein. In another embodiment, the rhodopsin protein is a bovine rhodopsin. In another embodiment, the cell comprises G α 15. In another embodiment, the polypeptide is expressed in a cell, and the polypeptide is contacted with the compound in the presence of a bitter tastant, wherein a difference in the functional effect of the bitter tastant on the cell in the presence of the compound and the functional effect of the bitter tastant on the cell in the absence of the compound indicates that the compound is capable of modulating taste signaling in taste cells.

In another embodiment, the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID

NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

In another aspect, the present invention provides an isolated nucleic acid encoding a taste transduction G-protein coupled receptor, the receptor comprising greater than about 50% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

In another aspect, the present invention provides an isolated nucleic acid encoding a taste transduction G-protein coupled receptor, wherein the nucleic acid is amplified by primers that selectively hybridize to the same sequence as degenerate primer sets encoding amino acid sequences selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

In another aspect, the present invention provides an isolated nucleic acid encoding a taste transduction G-protein coupled receptor, the receptor comprising greater than about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

In another aspect, the present invention provides an isolated nucleic acid encoding a taste transduction G-protein coupled receptor, wherein the nucleic acid specifically hybridizes under highly stringent conditions to a nucleic acid having a nucleotide sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID

NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165, but not to a nucleic acid having a nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, and SEQ ID NO:63.

15 In another aspect, the present invention provides an isolated nucleic acid encoding a taste transduction G-protein coupled receptor, the receptor comprising greater than about 60% amino acid identity to a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, wherein the nucleic acid selectively hybridizes under moderately stringent hybridization conditions to a nucleotide sequence having a nucleotide sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID

NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165 but not to a nucleic acid having a
5 nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID
10 NO:54, SEQ ID NO:57, SEQ ID NO:61, and SEQ ID NO:63.

In another aspect, the present invention provides an isolated nucleic acid encoding an extracellular domain or transmembrane region or a combination thereof of a taste transduction G-protein coupled receptor, the extracellular domain or transmembrane region having greater than about 60% amino acid sequence identity to the extracellular
15 domain or transmembrane region of a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID
20 NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ
25 ID NO:164.

In one embodiment, the nucleic acid encodes a receptor that specifically binds to polyclonal antibodies generated against a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID
30 NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID

NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, but not to polyclonal antibodies generated against a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76.

15 In another embodiment, the nucleic acid encodes a receptor comprising an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

30 In another embodiment, the nucleic acid comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID

NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165.

5 In another embodiment, the nucleic acid encodes a receptor that has G-protein coupled receptor activity. In another embodiment, the nucleic acid is from a rat or a mouse.

10 In another embodiment, the nucleic acid encodes an extracellular domain or transmembrane region or combination thereof linked to a heterologous polypeptide, forming a chimeric polypeptide. In another embodiment, the nucleic acid encodes the extracellular domain of a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

In another aspect, the present invention provides an expression vector comprising any of the above nucleic acids. In another aspect, the present invention provides isolated cells comprising the expression vector.

25 In another aspect, the present invention provides an isolated taste transduction G-protein coupled receptor, the receptor comprising greater than about 50% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

30 In another aspect, the present invention provides an isolated taste transduction G-protein coupled receptor, the receptor comprising greater than about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID

NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

In one embodiment, the receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

In another embodiment, the receptor specifically binds to polyclonal antibodies generated against a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, but not to polyclonal antibodies generated against a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ

NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171. In another embodiment, the extracellular domain or transmembrane region is covalently linked to a heterologous polypeptide, forming a chimeric polypeptide.

5 In one aspect, the present invention provides an antibody that selectively binds to the receptor comprising greater than about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID
10 NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID
15 NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

In another aspect, the present invention provides an expression vector comprising a nucleic acid encoding a taste transduction G-protein coupled receptor, wherein the receptor is expressed in a taste cell, the receptor comprising greater than
20 about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID
25 NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

30 In another aspect, the present invention provides a host cell transfected with the expression vector.

In another aspect, the present invention provides an expression cassette comprising a polynucleotide sequence that encodes a human taste transduction G protein coupled receptor, operably linked to a heterologous promoter, wherein the receptor

comprises an amino acid sequence comprising greater than about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76.

In one embodiment, the receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76.

In another aspect, the present invention provides an isolated eukaryotic cell comprising the expression cassette.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 demonstrates that $G\alpha 15$ couples the activation of μ opioid receptor and mGluR1 receptor to the release of intracellular calcium. HEK-293 cells were transiently transfected with the $G\alpha i$ coupled μ opioid receptor or the $G\alpha q$ coupled mGluR1 receptor. Transfected cells containing $G\alpha 15$ were assayed for increases in $[Ca^{2+}]_i$ before (a, b) and after (c, d) the addition of receptor agonists: (c) 10 μ M DAMGO

and (d) 20 μ M trans (\pm) 1-amino-1,3 cyclopentane dicarboxylic acid, (ACPD). Ligand- and receptor-dependent increase in $[Ca^{2+}]_i$ were dependent on $G\alpha 15$ (panels e, f). Scales indicate $[Ca^{2+}]_i$ (nM) determined from FURA-2 emission ratios.

Figure 2 shows that the first 39 amino acids of bovine rhodopsin effectively targets T2Rs to the plasma membrane of HEK-293 cells. Immunofluorescence staining of non-permeabilized cells transfected with representative rho-T2R fusions was detected using an anti-rhodopsin mAb B6-30.

Figure 3 demonstrates that T2R receptors are stimulated by bitter compounds. HEK-293 cells were transfected with rho-mT2R5 (a, d, g), rho-hT2R4 (b, e, h), and rho-mT2R8 (c, f, i). Cells expressing mT2R5 were stimulated using 1.5 μ M cycloheximide (d, g) and those expressing hT2R4 and mT2R8 with 1.5 mM denatonium (e, f, h, i). No increase in $[Ca^{2+}]_i$ was observed in the absence of $G\alpha 15$ (g - i); in contrast robust $G\alpha 15$ dependent responses were observed in the presence of tastants (d - f); scales indicate $[Ca^{2+}]_i$ (nM) determined from FURA-2 emission ratios. Line traces (j - l) show the kinetics of the $[Ca^{2+}]_i$ changes for representative cells from panels (d - f); arrows indicate addition of tastants.

Figure 4 shows that mT2R5 is a taste receptor for cycloheximide. (a) HEK-293 cells expressing $G\alpha 15$ and rho-mT2R5 were challenged with multiple pulses of 2 μ M cycloheximide (CYX), 3 mM 6-n-propyl thiouracil (PROP) or 5 mM denatonium (DEN); dots and horizontal bars above the traces indicate the time and duration of tastant pulses. Cycloheximide triggers robust receptor activation. This experiment also illustrates desensitization to repeated stimulation or during sustained application of the stimulus. (b) Responses to cycloheximide are highly specific and are not observed after addition of buffer (CON) or high concentrations of other tastants. Abbreviations and concentrations used are: cycloheximide, CYX (5 μ M); atropine, ATR (5 mM); brucine, BRU (5 mM); caffeic acid, CAFF (2 mM); denatonium, DEN (5 mM); epicatechin, (-)EPI (3 mM); phenyl thiocarbamide, PTC (3 mM); 6-n-propyl thiouracil, PROP (10 mM); saccharin, SAC (10 mM); strychnine, STR (5 mM); sucrose octaacetate, SOA (3 mM). Columns represent the mean \pm s.e of at least six independent experiments. (c) The mT2R5 gene from taster (DBA/2-allele) and non-taster (C57BL/6-allele) strains mediate differential $[Ca^{2+}]_i$ changes to pulses of cycloheximide. Horizontal bars depict the time and duration of the stimulus. 200 s was allowed to elapse between stimuli to ensure that cells were not desensitized due to the successive application of cycloheximide. (d)

Cycloheximide dose-response of mT2R5. Changes in $[Ca^{2+}]_i$ are shown as FURA-2 (F340/F380) ratios normalized to the response at 30 μ M cycloheximide; points represent the mean \pm s.e. of at least six determinations. The non-taster allele shows a marked decrease in cycloheximide sensitivity relative to the taster allele (EC50s of \sim 2.3 μ M versus 0.5 μ M, respectively).

Figure 5 shows that hT2R4 and mT2R8 respond to denatonium. HEK-293 cells expressing G α 15 were transiently transfected with hT2R4 or mT2R8 receptors and $[Ca^{2+}]_i$ was monitored as shown in Figure 3. (a) An increase in $[Ca^{2+}]_i$ could be induced by stimulation with denatonium but not by various other bitter compounds. Response profiles of (b) hT2R4 and (c) mT2R8 to a set of nine out of 55 different bitter and sweet tastants (see Experimental Procedures) are shown. CON refers to control buffer addition, NAR to 2mM naringin and LYS to 5mM lysine. Other abbreviations and concentrations are as reported in Figure 4. The mean FURA-2 fluorescence ratio (F340/F380) before and after ligand addition was obtained from 100 equal sized areas that included all responding cells. The values represent the mean \pm s.e. of at least 6 experiments.

Figure 6 demonstrates that cycloheximide taster and non-taster strains express different alleles of mT2R5. (a) Predicted transmembrane topology of mT2R5; amino-acid substitutions in the allele from non-taster strains are highlighted in red. The presence of only two alleles at this locus is not unexpected because the strains that share the same polymorphisms were derived from a common founder (Beck *et al.*, *Nat Genet* 24:23-55 (2000)). *In situ* hybridization showing expression of mT2R5 in subsets of cells in the circumvallate papilla of (b) a cycloheximide taster strain (DBA/2) and (c) a non-taster strain (C57BL/6); no strain specific differences in expression pattern were detected in taste buds from other regions of the oral cavity.

Figure 7 shows that mT2R5 activates gustducin in response to cycloheximide. (a) Insect larval cell membranes containing mT2R5 activate gustducin in the presence 300 μ M cycloheximide but not without ligand (control) or in the presence of 1 mM atropine, brucine, caffeine, denatonium, phenylthiocarbamide, 6-n-propyl thiouracil, quinine, saccharin, strychnine, sucrose octaacetate. (b) Cycloheximide concentration dependence of gustducin activation by mT2R5 was fitted by single-site binding ($K_d=14.8 \pm 0.9$ μ M).

Figure 8 provides a table including nucleic acid and protein sequences for a number of human, rat, and mouse T2R family members.

DETAILED DESCRIPTION OF THE INVENTION

5 I. Introduction

The present invention provides nucleic acids encoding a novel family of taste cell specific G-protein coupled receptors. These nucleic acids and the receptors that they encode are referred to as members of the “T2R” family of taste cell specific G protein coupled receptors. These taste cell specific GPCRs are components of the taste transduction pathway, *e.g.*, the bitter taste transduction pathway, and are involved in the taste detection of substances such as the bitter substances 6-n-propylthiouracil (PROP), sucrose octaacetate (soa), raffinose undecaacetate (roa), cycloheximide (cyx), denatonium, copper glycinate (Glb), and quinine (qui).

These nucleic acids provide valuable probes for the identification of taste cells, as the nucleic acids are specifically expressed in taste cells. For example, probes for T2R polypeptides and proteins can be used to identify taste cells present in foliate, circumvallate, and fungiform papillae, as well as taste cells present in the geschmackstreifen and epiglottis. In particular, T2R probes are useful to indentify bitter sensing, gustducin expressing taste cells. They also serve as tools for the generation of taste topographic maps that elucidate the relationship between the taste cells of the tongue and taste sensory neurons leading to taste centers in the brain. Furthermore, the nucleic acids and the proteins they encode can be used as probes to dissect taste-induced behaviors.

The invention also provides methods of screening for modulators, *e.g.*, activators, inhibitors, stimulators, enhancers, agonists, and antagonists, of these novel taste cell GPCRs. Such modulators of taste transduction are useful for pharmacological and genetic modulation of taste signaling pathways. These methods of screening can be used to identify high affinity agonists and antagonists of taste cell activity. These modulatory compounds can then be used in the food and pharmaceutical industries to customize taste, for example, to decrease the bitter taste of foods or drugs. Thus, the invention provides assays for taste modulation, where members of the T2R family act as direct or indirect reporter molecules for the effect of modulators on taste transduction. GPCRs can be used in assays, *e.g.*, to measure changes in ligand binding, ion concentration, membrane potential, current flow, ion flux, transcription, signal

transduction, receptor-ligand interactions, second messenger concentrations, *in vitro*, *in vivo*, and *ex vivo*. In one embodiment, members of the T2R family can be used as indirect reporters via attachment to a second reporter molecule such as green fluorescent protein (see, e.g., Mistili & Spector, *Nature Biotechnology* 15:961-964 (1997)). In another
5 embodiment, T2R family members are recombinantly expressed in cells, and modulation of taste transduction via GPCR activity is assayed by measuring changes in Ca^{2+} levels and other intracellular messages such as cAMP, cGMP, and IP3.

In a preferred embodiment, a T2R polypeptide is expressed in a eukaryotic cell as a chimeric receptor with a heterologous, chaperone sequence that facilitates its
10 maturation and targeting through the secretory pathway. In a preferred embodiment, the heterologous sequence is a rhodopsin sequence, such as an N-terminal fragment of a rhodopsin. Such chimeric T2R receptors can be expressed in any eukaryotic cell, such as HEK-293 cells. Preferably, the cells comprise a functional G protein, e.g., $\text{G}\alpha_{15}$, that is capable of coupling the chimeric receptor to an intracellular signaling pathway or to a
15 signaling protein such as phospholipase $\text{C}\beta$. Activation of such chimeric receptors in such cells can be detected using any standard method, such as by detecting changes in intracellular calcium by detecting FURA-2 dependent fluorescence in the cell.

Methods of assaying for modulators of taste transduction include *in vitro* ligand binding assays using T2R polypeptides, portions thereof such as the extracellular
20 domain or transmembrane region or combination thereof, or chimeric proteins comprising one or more domains of a T2R family member; oocyte or tissue culture cell T2R gene expression, or expression of T2R fragments or fusion proteins, such as rhodopsin fusion proteins; transcriptional activation of T2R genes; phosphorylation and dephosphorylation of T2R family members; G-protein binding to GPCRs; ligand binding assays; voltage,
25 membrane potential and conductance changes; ion flux assays; changes in intracellular second messengers such as cGMP, cAMP and inositol triphosphate; changes in intracellular calcium levels; and neurotransmitter release.

Finally, the invention provides methods of detecting T2R nucleic acid and protein expression, allowing investigation of taste transduction regulation and specific
30 identification of taste receptor cells. T2R family members also provide useful nucleic acid probes for paternity and forensic investigations. T2R genes are also useful as a nucleic acid probe for identifying taste receptor cells, such as foliate, fungiform, circumvallate, geschmackstreifen, and epiglottis taste receptor cells, in particular bitter-

taste receptive, gustducin expressing cells. T2R receptors can also be used to generate monoclonal and polyclonal antibodies useful for identifying taste receptor cells. Taste receptor cells can be identified using techniques such as reverse transcription and amplification of mRNA, isolation of total RNA or poly A⁺ RNA, northern blotting, dot blotting, *in situ* hybridization, RNase protection, S1 digestion, probing DNA microchip arrays, western blots, and the like.

The T2R genes comprise a large family of related taste cell specific G-protein coupled receptors. Within the genome, these genes are present either alone or within one of several gene clusters. One gene cluster, located at human genomic region 12p13, comprises at least 9 genes, and a second cluster, located at 7q31, comprises at least 4 genes. In total, more than 50 distinct T2R family members have been identified, including several putative pseudogenes. It is estimated that the human genome may contain as many as 80-120 distinct T2R genes, encoding as many as 40-80 functional human receptors.

Some of the T2R genes have been associated with previously mapped mammalian taste-specific loci. For example, the human T2R01 is located at human interval 5p15, precisely where the locus underlying the ability to taste the substance PROP has previously been mapped. In addition, the human gene cluster found at genomic region 12p13 corresponds to a region of mouse chromosome 6 that has been shown to contain numerous bitter-tasting genes, including sucrose octaacetate, ruffinose acetate, cycloheximide, and quinine (*see, e.g., Lush et al., Genet. Res. 6:167-174 (1995)*). These associations indicate that the T2R genes are involved in the taste detection of various substances, in particular bitter substances. In addition, as shown in Example 7, *infra*, mouse T2R5 is specifically receptive to cycloheximide, and mutations in the mT2R5 gene produce a Cyx phenotype. Similarly, human T2R 4 and mouse T2R8 are specifically receptive to both denatonium and PROP).

Functionally, the T2R genes comprise a family of related seven transmembrane G-protein coupled receptors involved in taste transduction, which interact with a G-protein to mediate taste signal transduction (*see, e.g., Fong, Cell Signal 8:217 (1996); Baldwin, Curr. Opin. Cell Biol. 6:180 (1994)*). In particular, T2Rs interact in a ligand-specific manner with the G protein Gustducin.

Structurally, the nucleotide sequence of T2R family members (*see, e.g., SEQ ID NOS:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 23, 25, 27, 29, 31, 34, 36, 38, 41, 43, 45, 52, 54, 57, 61, 63, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110,*

112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 157, 159, 161, 163, and 165, isolated from rats, mice, and humans) encodes a family of related polypeptides comprising an extracellular domain, seven transmembrane domains, and a cytoplasmic domain. Related T2R family genes from other species share at least about 60% nucleotide sequence identity over a region of at least about 50 nucleotides in length, optionally 100, 200, 500, or more nucleotides in length, to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 23, 25, 27, 29, 31, 34, 36, 38, 41, 43, 45, 52, 54, 57, 61, 63, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 157, 159, 161, 163, or 165, or encode polypeptides sharing at least about 60% amino acid sequence identity over an amino acid region at least about 25 amino acids in length, optionally 50 to 100 amino acids in length to SEQ ID NO:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 22, 24, 26, 28, 30, 32, 33, 35, 37, 39, 40, 42, 44, 46-51, 53, 55, 56, 58-60, 62, 64-77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 158, 160, 162, or 164. T2R genes are specifically expressed in taste cells.

Several consensus amino acid sequences or domains have also been identified that are characteristic of T2R family members. For example, T2R family members typically comprise a sequence having at least about 50%, optionally 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or higher, identity to SEQ ID NO:166 (corresponding, *e.g.*, to amino acid positions 16-35 in SEQ ID NO:1, and to T2R transmembrane region 1), SEQ ID NO:167 (corresponding, *e.g.*, to amino acid positions 45-58 in SEQ ID NO:1, and to T2R transmembrane region 2), SEQ ID NO:168 (corresponding, *e.g.*, to amino acid positions 89-101 in SEQ ID NO:1, and to T2R transmembrane region 3), SEQ ID NO:169 (corresponding, *e.g.*, to amino acid positions 102-119 in SEQ ID NO:1, and to T2R transmembrane region 3), SEQ ID NO:170 (corresponding, *e.g.*, to amino acid positions 196-209 in SEQ ID NO:1, and to T2R transmembrane region 5), or SEQ ID NO:171 (corresponding, *e.g.*, to amino acid positions 273-286 in SEQ ID NO:35, and to T2R transmembrane region 7). These conserved domains thus can be used to identify members of the T2R family, by % identity, specific hybridization or amplification, or specific binding by antibodies raised against a domain.

Several T2R genes represent apparent orthologs of each other. For example, human T2R01 (SEQ ID NOs:1, 2), rat T2R01 (SEQ ID NOs:77, 78), and mouse T2R19 (SEQ ID NOs:141, 142), are apparent orthologs. In addition, rat T2R08 (SEQ ID NOs:91, 92) and mouse T2R02 (SEQ ID NOs:107, 108) are about 74% identical at the amino acid sequence level, and are each at least about 50% identical to human T2R13 (SEQ ID NOs:24, 25). Rat T2R03 (SEQ ID NOs:81, 82) and mouse T2R18 (SEQ ID NOs:139, 140) are about 92% identical, and are each at least about 50% identical to human T2R16 (SEQ ID NOs:30, 31). Finally, human T2R04 (SEQ ID NOs:7, 8) and mouse T2R08 (SEQ ID NOs:119, 120) are about 67% identical to each other.

The present invention also provides polymorphic variants of the T2R proteins provided herein. For example, in the rat T2R depicted in SEQ ID NO:77: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 7; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 20.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:79: variant #1, in which a tyrosine residue is substituted for a phenylalanine residue at amino acid position 2; and variant #2, in which a valine residue is substituted for an isoleucine residue at amino acid position 62.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:81: variant #1, in which a glutamine residue is substituted for an asparagine residue at amino acid position 179; and variant #2, in which a cysteine residue is substituted for a methionine residue at amino acid position 183.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:83: variant #1, in which a glycine residue is substituted for an alanine residue at amino acid position 4; and variant #2, in which a leucine residue is substituted for an isoleucine residue at amino acid position 63.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:85: variant #1, in which a valine residue is substituted for an isoleucine residue at amino acid position 56; and variant #2, in which a methionine residue is substituted for a cysteine residue at amino acid position 57.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:87: variant #1, in which an isoleucine residue is substituted for a valine residue at amino acid position 4; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 5.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:89: variant #1, in which an alanine residue is substituted for a glycine residue at amino acid position 79; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 127.

5 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:91: variant #1, in which a leucine residue is substituted for a valine residue at amino acid position 28; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 80.

10 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:93: variant #1, in which an arginine residue is substituted for a lysine residue at amino acid position 75; and variant #2, in which a methionine residue is substituted for a cysteine residue at amino acid position 251.

15 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:95: variant #1, in which a threonine residue is substituted for a serine residue at amino acid position 48; and variant #2, in which an isoleucine residue is substituted for a valine residue at amino acid position 49.

20 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:97: variant #1, in which a glutamic acid residue is substituted for an aspartic acid residue at amino acid position 25; and variant #2, in which an isoleucine residue is substituted for a leucine residue at amino acid position 100.

25 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:99: variant #1, in which a serine residue is substituted for a threonine residue at amino acid position 4; and variant #2, in which an isoleucine residue is substituted for a valine residue at amino acid position 74.

 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:101: variant #1, in which an asparagine residue is substituted for a glutamine residue at amino acid position 9; and variant #2, in which a tryptophan residue is substituted for a tyrosine residue at amino acid position 18.

30 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:103: variant #1, in which a threonine residue is substituted for a serine residue at amino acid position 26; and variant #2, in which an isoleucine residue is substituted for a valine residue at amino acid position 8.

 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:105: variant #1, in which an isoleucine residue is

substituted for a leucine residue at amino acid position 4; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 46.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:107: variant #1, in which a threonine residue is substituted for a serine residue at amino acid position 3; and variant #2, in which an isoleucine residue is substituted for a valine residue at amino acid position 28.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:109: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 26; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 50.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:111: variant #1, in which a glycine residue is substituted for an alanine residue at amino acid position 4; and variant #2, in which a phenylalanine residue is substituted for a tryptophan residue at amino acid position 60.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:113: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 62; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 244.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:115: variant #1, in which a serine residue is substituted for a threonine residue at amino acid position 3; and variant #2, in which a lysine residue is substituted for an arginine residue at amino acid position 123.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:117: variant #1, in which an asparagine residue is substituted for a glutamine residue at amino acid position 65; and variant #2, in which a leucine residue is substituted for an isoleucine residue at amino acid position 68.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:119: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 2; and variant #2, in which an aspartic acid residue is substituted for a glutamic acid residue at amino acid position 4.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:121: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 16; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 46.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:123: variant #1, in which a threonine residue is substituted for a serine residue at amino acid position 9; and variant #2, in which a tryptophan residue is substituted for a phenylalanine residue at amino acid position 14.

5 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:125: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 24; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 53.

10 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:127: variant #1, in which a phenylalanine residue is substituted for a tryptophan residue at amino acid position 51; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 101.

15 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:129: variant #1, in which an isoleucine residue is substituted for a valine residue at amino acid position 4; and variant #2, in which a glycine residue is substituted for an alanine residue at amino acid position 52.

20 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:131: variant #1, in which an arginine residue is substituted for a lysine residue at amino acid position 150; and variant #2, in which a leucine residue is substituted for a valine residue at amino acid position 225.

25 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:133: variant #1, in which a leucine residue is substituted for an isoleucine residue at amino acid position 27; and variant #2, in which a lysine residue is substituted for an arginine residue at amino acid position 127.

30 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:135: variant #1, in which a threonine residue is substituted for a serine residue at amino acid position 102; and variant #2, in which a glutamic acid residue is substituted for an aspartic acid residue at amino acid position 220.

 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:137: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 24; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 45.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:139: variant #1, in which a leucine residue is substituted for an isoleucine residue at amino acid position 50; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 53.

5 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:141: variant #1, in which a serine residue is substituted for a threonine residue at amino acid position 76; and variant #2, in which an isoleucine residue is substituted for a leucine residue at amino acid position 131.

10 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:143: variant #1, in which an alanine residue is substituted for a glycine residue at amino acid position 98; and variant #2, in which a phenylalanine residue is substituted for a tryptophan residue at amino acid position 153.

15 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:145: variant #1, in which a leucine residue is substituted for an isoleucine residue at amino acid position 8; and variant #2, in which a glycine residue is substituted for an alanine residue at amino acid position 100.

20 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:147: variant #1, in which a glycine residue is substituted for an alanine residue at amino acid position 52; and variant #2, in which a valine residue is substituted for a leucine residue at amino acid position 75.

 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:149: variant #1, in which a lysine residue is substituted for an arginine residue at amino acid position 44; and variant #2, in which a leucine residue is substituted for a valine residue at amino acid position 49.

25 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:151: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 5; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 25.

30 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:153: variant #1, in which a glutamic acid residue is substituted for an aspartic acid residue at amino acid position 7; and variant #2, in which an isoleucine residue is substituted for a leucine residue at amino acid position 60.

 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:155: variant #1, in which an isoleucine residue is

substituted for a valine residue at amino acid position 7; and variant #2, in which a glycine residue is substituted for an alanine residue at amino acid position 23.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:158: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 5; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 21.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:160: variant #1, in which a leucine residue is substituted for a valine residue at amino acid position 5; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 23.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:162: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 22; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 34.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:164: variant #1, in which a leucine residue is substituted for an isoleucine residue at amino acid position 49; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 76.

Specific regions of the T2R nucleotide and amino acid sequences may be used to identify polymorphic variants, interspecies homologs, and alleles of T2R family members. This identification can be made *in vitro*, *e.g.*, under stringent hybridization conditions or PCR (*e.g.*, using primers encoding SEQ ID NOS:166-171) and sequencing, or by using the sequence information in a computer system for comparison with other nucleotide sequences. Typically, identification of polymorphic variants and alleles of T2R family members is made by comparing an amino acid sequence of about 25 amino acids or more, *e.g.*, 50-100 amino acids. Amino acid identity of approximately at least 60% or above, optionally 65%, 70%, 75%, 80%, 85%, or 90-95% or above typically demonstrates that a protein is a polymorphic variant, interspecies homolog, or allele of a T2R family member. Sequence comparison can be performed using any of the sequence comparison algorithms discussed below. Antibodies that bind specifically to T2R polypeptides or a conserved region thereof can also be used to identify alleles, interspecies homologs, and polymorphic variants.

Polymorphic variants, interspecies homologs, and alleles of T2R genes are confirmed by examining taste cell specific expression of the putative T2R polypeptide.

Typically, T2R polypeptides having an amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, or SEQ ID NO:164 is used as a positive control in comparison to the putative T2R protein to demonstrate the identification of a polymorphic variant or allele of the T2R family member. The polymorphic variants, alleles and interspecies homologs are expected to retain the seven transmembrane structure of a G-protein coupled receptor.

The present invention also provides nucleotide sequences for T2R promoters, which can be used to drive taste cell-specific expression of polynucleotides, especially in gustducin expressing taste cells that are receptive to bitter tastants.

Nucleotide and amino acid sequence information for T2R family members may also be used to construct models of taste cell specific polypeptides in a computer system. These models are subsequently used to identify compounds that can activate or inhibit T2R receptor proteins. Such compounds that modulate the activity of T2R family members can be used to investigate the role of T2R genes in taste transduction.

The isolation of T2R family members provides a means for assaying for inhibitors and activators of G-protein coupled receptor taste transduction. Biologically active T2R proteins are useful for testing inhibitors and activators of T2R as taste

transducers, especially bitter taste transducers, using *in vivo* and *in vitro* assays that measure, *e.g.*, transcriptional activation of T2R-dependent genes; ligand binding; phosphorylation and dephosphorylation; binding to G-proteins; G-protein activation; regulatory molecule binding; voltage, membrane potential and conductance changes; ion
5 flux; intracellular second messengers such as cGMP, cAMP and inositol triphosphate; intracellular calcium levels; and neurotransmitter release. Such activators and inhibitors identified using T2R family members can be used to further study taste transduction and to identify specific taste agonists and antagonists. Such activators and inhibitors are useful as pharmaceutical and food agents for customizing taste, for example to decrease
10 the bitter taste of foods or pharmaceuticals.

The present invention also provides assays, preferably high throughput assays, to identify molecules that interact with and/or modulate a T2R polypeptide. In numerous assays, a particular domain of a T2R family member is used, *e.g.*, an extracellular, transmembrane, or intracellular domain or region. In numerous
15 embodiments, an extracellular domain or transmembrane region or combination thereof is bound to a solid substrate, and used, *e.g.*, to isolate ligands, agonists, antagonists, or any other molecule that can bind to and/or modulate the activity of an extracellular domain or transmembrane region of a T2R polypeptide. In certain embodiments, a domain of a T2R polypeptide, *e.g.*, an extracellular, transmembrane, or intracellular domain, is fused to a
20 heterologous polypeptide, thereby forming a chimeric polypeptide, *e.g.*, a chimeric polypeptide with G protein coupled receptor activity. Such chimeric polypeptides are useful, *e.g.*, in assays to identify ligands, agonists, antagonists, or other modulators of a T2R polypeptide. In addition, such chimeric polypeptides are useful to create novel taste receptors with novel ligand binding specificity, modes of regulation, signal transduction
25 pathways, or other such properties, or to create novel taste receptors with novel combinations of ligand binding specificity, modes of regulation, signal transduction pathways, *etc.*

Methods of detecting T2R nucleic acids and expression of T2R polypeptides are also useful for identifying taste cells and creating topological maps of
30 the tongue and the relation of tongue taste receptor cells to taste sensory neurons in the brain. In particular, methods of detecting T2R can be used to identify taste cells sensitive to bitter tastants. Chromosome localization of the genes encoding human T2R genes can be used to identify diseases, mutations, and traits caused by and associated with T2R family members.

II. Definitions

As used herein, the following terms have the meanings ascribed to them unless specified otherwise.

5 “Taste cells” include neuroepithelial cells that are organized into groups to form taste buds of the tongue, *e.g.*, foliate, fungiform, and circumvallate cells (*see, e.g.*, Roper *et al.*, *Ann. Rev. Neurosci.* 12:329-353 (1989)). Taste cells also include cells of the palate, and other tissues that may contain taste cells such as the esophagus and the stomach.

10 “T2R” refers to one or more members of a family of G-protein coupled receptors that are expressed in taste cells such as foliate, fungiform, and circumvallate cells, as well as cells of the palate, esophagus, and stomach (*see, e.g.*, Hoon *et al.*, *Cell* 96:541-551 (1999), herein incorporated by reference in its entirety). This family is also referred to as the “SF family” (*see, e.g.*, USSN 09/393,634). Such taste cells can be
15 identified because they express specific molecules such as Gustducin, a taste cell specific G protein, or other taste specific molecules (McLaughlin *et al.*, *Nature* 357:563-569 (1992)). Taste receptor cells can also be identified on the basis of morphology (*see, e.g.*, Roper, *supra*). T2R family members have the ability to act as receptors for taste transduction. T2R family members are also referred to as the “GR” family, for gustatory
20 receptor, or “SF” family.

 “T2R” nucleic acids encode a family of GPCRs with seven transmembrane regions that have “G-protein coupled receptor activity,” *e.g.*, they bind to G-proteins in response to extracellular stimuli and promote production of second messengers such as IP3, cAMP, cGMP, and Ca²⁺ via stimulation of enzymes such as phospholipase C and
25 adenylate cyclase (for a description of the structure and function of GPCRs, *see, e.g.*, Fong, *supra*, and Baldwin, *supra*). A dendogram providing the relationship between certain T2R family members is provided as Figure 2. These nucleic acids encode proteins that are expressed in taste cells, in particular Gustducin-expressing taste cells that are responsive to bitter tastants. A single taste cell may contain many distinct T2R
30 polypeptides.

 The term “T2R” family therefore refers to polymorphic variants, alleles, mutants, and interspecies homologs that: (1) have about 60% amino acid sequence identity, optionally about 75, 80, 85, 90, or 95% amino acid sequence identity to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ

ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID
 NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID
 NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID
 NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID
 5 NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID
 NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID
 NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID
 NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID
 NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID
 10 NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID
 NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID
 NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID
 NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID
 NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID
 15 NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID
 NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID
 NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID
 NO:160, SEQ ID NO:162, or SEQ ID NO:164 over a window of about 25 amino acids,
 optionally 50-100 amino acids; (2) specifically bind to antibodies raised against an
 20 immunogen comprising an amino acid sequence selected from the group consisting of
 SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID
 NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID
 NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID
 NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID
 25 NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID
 NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID
 NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID
 NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID
 NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID
 30 NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID
 NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID
 NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID
 NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID
 NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID

NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, and conservatively modified variants thereof; (3) specifically hybridize (with a size of at least about 100, optionally at least about 500-1000 nucleotides) under stringent hybridization conditions to a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165, and conservatively modified variants thereof; (4) comprise a sequence at least about 50% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171; or (5) are amplified by primers that specifically hybridize under stringent hybridization conditions to the same sequence as a degenerate primer sets encoding SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, or SEQ ID NO:171.

Topologically, sensory GPCRs have an “N-terminal domain” “extracellular domains,” a “transmembrane domain” comprising seven transmembrane regions, cytoplasmic, and extracellular loops, “cytoplasmic domains,” and a “C-terminal domain” (*see, e.g., Hoon et al., Cell* 96:541-551 (1999); Buck & Axel, *Cell* 65:175-187 (1991)). These domains can be structurally identified using methods known to those of

skill in the art, such as sequence analysis programs that identify hydrophobic and hydrophilic domains (*see, e.g., Stryer, Biochemistry* (3rd ed. 1988); *see also* any of a number of Internet based sequence analysis programs, such as those found at dot.imgen.bcm.tmc.edu). Such domains are useful for making chimeric proteins and for
5 *in vitro* assays of the invention, *e.g.,* ligand binding assays.

“Extracellular domains” therefore refers to the domains of T2R polypeptides that protrude from the cellular membrane and are exposed to the extracellular face of the cell. Such domains would include the “N terminal domain” that is exposed to the extracellular face of the cell, as well as the extracellular loops of the
10 transmembrane domain that are exposed to the extracellular face of the cell, *i.e.,* the loops between transmembrane regions 2 and 3, and between transmembrane regions 4 and 5. The “N terminal domain” region starts at the N-terminus and extends to a region close to the start of the transmembrane domain. These extracellular domains are useful for *in vitro* ligand binding assays, both soluble and solid phase. In addition, transmembrane
15 regions, described below, can also bind ligand either in combination with the extracellular domain or alone, and are therefore also useful for *in vitro* ligand binding assays.

“Transmembrane domain,” which comprises the seven transmembrane “regions,” refers to the domain of T2R polypeptides that lies within the plasma membrane, and may also include the corresponding cytoplasmic (intracellular) and
20 extracellular loops, also referred to as transmembrane domain “regions.” The seven transmembrane regions and extracellular and cytoplasmic loops can be identified using standard methods, as described in Kyte & Doolittle, *J. Mol. Biol.* 157:105-132 (1982)), or in Stryer, *supra*.

“Cytoplasmic domains” refers to the domains of T2R proteins that face the
25 inside of the cell, *e.g.,* the “C terminal domain” and the intracellular loops of the transmembrane domain, *e.g.,* the intracellular loops between transmembrane regions 1 and 2, and the intracellular loops between transmembrane regions 3 and 4. “C terminal domain” refers to the region that spans the end of the last transmembrane domain and the C-terminus of the protein, and which is normally located within the cytoplasm.

30 “Biological sample” as used herein is a sample of biological tissue or fluid that contains one or more T2R nucleic acids encoding one or more T2R proteins. Such samples include, but are not limited to, tissue isolated from humans, mice, and rats, in particular, tongue, palate, and other tissues that may contain taste cells such as the esophagus and the stomach. Biological samples may also include sections of tissues such

as frozen sections taken for histological purposes. A biological sample is typically obtained from a eukaryotic organism, such as insects, protozoa, birds, fish, reptiles, and preferably a mammal such as rat, mouse, cow, dog, guinea pig, or rabbit, and most preferably a primate such as chimpanzees or humans.

5 “GPCR activity” refers to the ability of a GPCR to transduce a signal. Such activity can be measured in a heterologous cell, by coupling a GPCR (or a chimeric GPCR) to either a G-protein or promiscuous G-protein such as Gα15, and an enzyme such as PLC, and measuring increases in intracellular calcium using (Offermans & Simon, *J. Biol. Chem.* 270:15175-15180 (1995)). Receptor activity can be effectively
10 measured by recording ligand-induced changes in $[Ca^{2+}]_i$ using fluorescent Ca^{2+} -indicator dyes and fluorometric imaging. Optionally, the polypeptides of the invention are involved in sensory transduction, optionally taste transduction in taste cells.

 The phrase “functional effects” in the context of assays for testing compounds that modulate T2R family member mediated taste transduction includes the
15 determination of any parameter that is indirectly or directly under the influence of the receptor, *e.g.*, functional, physical and chemical effects. It includes ligand binding, changes in ion flux, membrane potential, current flow, transcription, G-protein binding, GPCR phosphorylation or dephosphorylation, signal transduction, receptor-ligand interactions, second messenger concentrations (*e.g.*, cAMP, cGMP, IP3, or intracellular
20 Ca^{2+}), *in vitro*, *in vivo*, and *ex vivo* and also includes other physiologic effects such increases or decreases of neurotransmitter or hormone release.

 By “determining the functional effect” is meant assays for a compound that increases or decreases a parameter that is indirectly or directly under the influence of a T2R family member, *e.g.*, functional, physical and chemical effects. Such functional
25 effects can be measured by any means known to those skilled in the art, *e.g.*, changes in spectroscopic characteristics (*e.g.*, fluorescence, absorbance, refractive index), hydrodynamic (*e.g.*, shape), chromatographic, or solubility properties, patch clamping, voltage-sensitive dyes, whole cell currents, radioisotope efflux, inducible markers, oocyte T2R gene expression; tissue culture cell T2R expression; transcriptional activation of
30 T2R genes; ligand binding assays; voltage, membrane potential and conductance changes; ion flux assays; changes in intracellular second messengers such as cAMP, cGMP, and inositol triphosphate (IP3); changes in intracellular calcium levels; neurotransmitter release, and the like.

“Inhibitors,” “activators,” and “modulators” of T2R genes or proteins are used interchangeably to refer to inhibitory, activating, or modulating molecules identified using *in vitro* and *in vivo* assays for taste transduction, *e.g.*, ligands, agonists, antagonists, and their homologs and mimetics. Inhibitors are compounds that, *e.g.*, bind to, partially or totally block stimulation, decrease, prevent, delay activation, inactivate, desensitize, or down regulate taste transduction, *e.g.*, antagonists. Activators are compounds that, *e.g.*, bind to, stimulate, increase, open, activate, facilitate, enhance activation, sensitize or up regulate taste transduction, *e.g.*, agonists. Modulators include compounds that, *e.g.*, alter the interaction of a receptor with: extracellular proteins that bind activators or inhibitor (*e.g.*, ebnerin and other members of the hydrophobic carrier family); G -proteins; kinases (*e.g.*, homologs of rhodopsin kinase and beta adrenergic receptor kinases that are involved in deactivation and desensitization of a receptor); and arrestin-like proteins, which also deactivate and desensitize receptors. Modulators include genetically modified versions of T2R family members, *e.g.*, with altered activity, as well as naturally occurring and synthetic ligands, antagonists, agonists, small chemical molecules and the like. Such assays for inhibitors and activators include, *e.g.*, expressing T2R family members in cells or cell membranes, applying putative modulator compounds, in the presence or absence of tastants, *e.g.*, bitter tastants, and then determining the functional effects on taste transduction, as described above. Samples or assays comprising T2R family members that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of inhibition. Control samples (untreated with inhibitors) are assigned a relative T2R activity value of 100%. Inhibition of a T2R is achieved when the T2R activity value relative to the control is about 80%, optionally 50% or 25-0%. Activation of a T2R is achieved when the T2R activity value relative to the control is 110%, optionally 150%, optionally 200-500%, or 1000-3000% higher.

“Biologically active” T2R refers to a T2R having GPCR activity as described above, involved in taste transduction in taste receptor cells, in particular bitter taste transduction.

The terms “isolated” “purified” or “biologically pure” refer to material that is substantially or essentially free from components which normally accompany it as found in its native state. Purity and homogeneity are typically determined using analytical chemistry techniques such as polyacrylamide gel electrophoresis or high performance liquid chromatography. A protein that is the predominant species present in

a preparation is substantially purified. In particular, an isolated T2R nucleic acid is separated from open reading frames that flank the T2R gene and encode proteins other than a T2R. The term “purified” denotes that a nucleic acid or protein gives rise to essentially one band in an electrophoretic gel. Particularly, it means that the nucleic acid or protein is at least 85% pure, optionally at least 95% pure, and optionally at least 99% pure.

“Nucleic acid” refers to deoxyribonucleotides or ribonucleotides and polymers thereof in either single- or double-stranded form. The term encompasses nucleic acids containing known nucleotide analogs or modified backbone residues or linkages, which are synthetic, naturally occurring, and non-naturally occurring, which have similar binding properties as the reference nucleic acid, and which are metabolized in a manner similar to the reference nucleotides. Examples of such analogs include, without limitation, phosphorothioates, phosphoramidates, methyl phosphonates, chiral-methyl phosphonates, 2-O-methyl ribonucleotides, peptide-nucleic acids (PNAs).

Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (*e.g.*, degenerate codon substitutions) and complementary sequences, as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer *et al.*, *Nucleic Acid Res.* 19:5081 (1991); Ohtsuka *et al.*, *J. Biol. Chem.* 260:2605-2608 (1985); Rossolini *et al.*, *Mol. Cell. Probes* 8:91-98 (1994)). The term nucleic acid is used interchangeably with gene, cDNA, mRNA, oligonucleotide, and polynucleotide.

The terms “polypeptide,” “peptide” and “protein” are used interchangeably herein to refer to a polymer of amino acid residues. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers and non-naturally occurring amino acid polymer.

The term “amino acid” refers to naturally occurring and synthetic amino acids, as well as amino acid analogs and amino acid mimetics that function in a manner similar to the naturally occurring amino acids. Naturally occurring amino acids are those encoded by the genetic code, as well as those amino acids that are later modified, *e.g.*, hydroxyproline, γ -carboxyglutamate, and O-phosphoserine. Amino acid analogs refers to compounds that have the same basic chemical structure as a naturally occurring amino

acid, *i.e.*, an α carbon that is bound to a hydrogen, a carboxyl group, an amino group, and an R group, *e.g.*, homoserine, norleucine, methionine sulfoxide, methionine methyl sulfonium. Such analogs have modified R groups (*e.g.*, norleucine) or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid. Amino acid mimetics refers to chemical compounds that have a structure that is different from the general chemical structure of an amino acid, but that functions in a manner similar to a naturally occurring amino acid.

Amino acids may be referred to herein by either their commonly known three letter symbols or by the one-letter symbols recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Nucleotides, likewise, may be referred to by their commonly accepted single-letter codes.

“Conservatively modified variants” applies to both amino acid and nucleic acid sequences. With respect to particular nucleic acid sequences, conservatively modified variants refers to those nucleic acids which encode identical or essentially identical amino acid sequences, or where the nucleic acid does not encode an amino acid sequence, to essentially identical sequences. Because of the degeneracy of the genetic code, a large number of functionally identical nucleic acids encode any given protein. For instance, the codons GCA, GCC, GCG and GCU all encode the amino acid alanine. Thus, at every position where an alanine is specified by a codon, the codon can be altered to any of the corresponding codons described without altering the encoded polypeptide. Such nucleic acid variations are “silent variations,” which are one species of conservatively modified variations. Every nucleic acid sequence herein which encodes a polypeptide also describes every possible silent variation of the nucleic acid. One of skill will recognize that each codon in a nucleic acid (except AUG, which is ordinarily the only codon for methionine, and TGG, which is ordinarily the only codon for tryptophan) can be modified to yield a functionally identical molecule. Accordingly, each silent variation of a nucleic acid which encodes a polypeptide is implicit in each described sequence.

As to amino acid sequences, one of skill will recognize that individual substitutions, deletions or additions to a nucleic acid, peptide, polypeptide, or protein sequence which alters, adds or deletes a single amino acid or a small percentage of amino acids in the encoded sequence is a “conservatively modified variant” where the alteration results in the substitution of an amino acid with a chemically similar amino acid. Conservative substitution tables providing functionally similar amino acids are well

known in the art. Such conservatively modified variants are in addition to and do not exclude polymorphic variants, interspecies homologs, and alleles of the invention.

The following eight groups each contain amino acids that are conservative substitutions for one another:

- 5 1) Alanine (A), Glycine (G);
 - 2) Aspartic acid (D), Glutamic acid (E);
 - 3) Asparagine (N), Glutamine (Q);
 - 4) Arginine (R), Lysine (K);
 - 5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V);
 - 10 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W);
 - 7) Serine (S), Threonine (T); and
 - 8) Cysteine (C), Methionine (M)
- (see, e.g., Creighton, *Proteins* (1984)).

- Macromolecular structures such as polypeptide structures can be described
- 15 in terms of various levels of organization. For a general discussion of this organization, see, e.g., Alberts *et al.*, *Molecular Biology of the Cell* (3rd ed., 1994) and Cantor and Schimmel, *Biophysical Chemistry Part I: The Conformation of Biological*
- 20 *Macromolecules* (1980). “Primary structure” refers to the amino acid sequence of a particular peptide. “Secondary structure” refers to locally ordered, three dimensional structures within a polypeptide. These structures are commonly known as domains. Domains are portions of a polypeptide that form a compact unit of the polypeptide and are typically 50 to 350 amino acids long. Typical domains are made up of sections of lesser organization such as stretches of β -sheet and α -helices. “Tertiary structure” refers to the complete three dimensional structure of a polypeptide monomer. “Quaternary
- 25 structure” refers to the three dimensional structure formed by the noncovalent association of independent tertiary units. Anisotropic terms are also known as energy terms.

- A “label” or a “detectable moiety” is a composition detectable by spectroscopic, photochemical, biochemical, immunochemical, or chemical means. For example, useful labels include ^{32}P , fluorescent dyes, electron-dense reagents, enzymes
- 30 (e.g., as commonly used in an ELISA), biotin, digoxigenin, or haptens and proteins which can be made detectable, e.g., by incorporating a radiolabel into the peptide or used to detect antibodies specifically reactive with the peptide.

A “labeled nucleic acid probe or oligonucleotide” is one that is bound, either covalently, through a linker or a chemical bond, or noncovalently, through ionic, van der Waals, electrostatic, or hydrogen bonds to a label such that the presence of the probe may be detected by detecting the presence of the label bound to the probe.

5 As used herein a “nucleic acid probe or oligonucleotide” is defined as a nucleic acid capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation. As used herein, a probe may include natural (*i.e.*, A, G, C, or T) or modified bases (7-deazaguanosine, inosine, *etc.*). In
10 addition, the bases in a probe may be joined by a linkage other than a phosphodiester bond, so long as it does not interfere with hybridization. Thus, for example, probes may be peptide nucleic acids in which the constituent bases are joined by peptide bonds rather than phosphodiester linkages. It will be understood by one of skill in the art that probes may bind target sequences lacking complete complementarity with the probe sequence
15 depending upon the stringency of the hybridization conditions. The probes are optionally directly labeled as with isotopes, chromophores, lumiphores, chromogens, or indirectly labeled such as with biotin to which a streptavidin complex may later bind. By assaying for the presence or absence of the probe, one can detect the presence or absence of the select sequence or subsequence.

20 The term “recombinant” when used with reference, *e.g.*, to a cell, or nucleic acid, protein, or vector, indicates that the cell, nucleic acid, protein or vector, has been modified by the introduction of a heterologous nucleic acid or protein or the alteration of a native nucleic acid or protein, or that the cell is derived from a cell so modified. Thus, for example, recombinant cells express genes that are not found within
25 the native (non-recombinant) form of the cell or express native genes that are otherwise abnormally expressed, under expressed or not expressed at all.

The term “heterologous” when used with reference to portions of a nucleic acid indicates that the nucleic acid comprises two or more subsequences that are not found in the same relationship to each other in nature. For instance, the nucleic acid is
30 typically recombinantly produced, having two or more sequences from unrelated genes arranged to make a new functional nucleic acid, *e.g.*, a promoter from one source and a coding region from another source. Similarly, a heterologous protein indicates that the protein comprises two or more subsequences that are not found in the same relationship to each other in nature (*e.g.*, a fusion protein).

A “promoter” is defined as an array of nucleic acid control sequences that direct transcription of a nucleic acid. As used herein, a promoter includes necessary nucleic acid sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes
5 distal enhancer or repressor elements, which can be located as much as several thousand base pairs from the start site of transcription. A “constitutive” promoter is a promoter that is active under most environmental and developmental conditions. An “inducible” promoter is a promoter that is active under environmental or developmental regulation. The term “operably linked” refers to a functional linkage between a nucleic acid
10 expression control sequence (such as a promoter, or array of transcription factor binding sites) and a second nucleic acid sequence, wherein the expression control sequence directs transcription of the nucleic acid corresponding to the second sequence.

An “expression vector” is a nucleic acid construct, generated recombinantly or synthetically, with a series of specified nucleic acid elements that
15 permit transcription of a particular nucleic acid in a host cell. The expression vector can be part of a plasmid, virus, or nucleic acid fragment. Typically, the expression vector includes a nucleic acid to be transcribed operably linked to a promoter.

The terms “identical” or percent “identity,” in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences
20 or domains that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (*i.e.*, 50% identity, optionally 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or higher identity over a specified region), when compared and aligned for maximum correspondence over a comparison window, or designated region as measured using one of the following sequence comparison algorithms or by manual
25 alignment and visual inspection. Such sequences are then said to be “substantially identical.” This definition also refers to the complement of a test sequence. Optionally, the identity exists over a region that is at least about 50 amino acids or nucleotides in length, or more preferably over a region that is 75-100 amino acids or nucleotides in length.

30 For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Default program parameters can be used, as described below for the

BLASTN and BLASTP programs, or alternative parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters.

A “comparison window”, as used herein, includes reference to a segment
5 of any one of the number of contiguous positions selected from the group consisting of from 20 to 600, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Methods of alignment of sequences for comparison are well-known in the art. Optimal alignment of
10 sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, *J. Mol. Biol.* 48:443 (1970), by the search for similarity method of Pearson & Lipman, *Proc. Nat’l. Acad. Sci. USA* 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and
15 TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by manual alignment and visual inspection (*see, e.g., Current Protocols in Molecular Biology* (Ausubel *et al.*, eds. 1995 supplement)).

A preferred example of an algorithm that is suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0
20 algorithms, which are described in Altschul *et al.*, *Nuc. Acids Res.* 25:3389-3402 (1977) and Altschul *et al.*, *J. Mol. Biol.* 215:403-410 (1990), respectively. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in
25 the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the
30 cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by

the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for
5 nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (*see* Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915 (1989)) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a
10 comparison of both strands.

Another example of a useful algorithm is PILEUP. PILEUP creates a multiple sequence alignment from a group of related sequences using progressive, pairwise alignments to show relationship and percent sequence identity. It also plots a tree or dendrogram showing the clustering relationships used to create the alignment (*see*,
15 *e.g.*, Figure 2). PILEUP uses a simplification of the progressive alignment method of Feng & Doolittle, *J. Mol. Evol.* 35:351-360 (1987). The method used is similar to the method described by Higgins & Sharp, *CABIOS* 5:151-153 (1989). The program can align up to 300 sequences, each of a maximum length of 5,000 nucleotides or amino acids. The multiple alignment procedure begins with the pairwise alignment of the two
20 most similar sequences, producing a cluster of two aligned sequences. This cluster is then aligned to the next most related sequence or cluster of aligned sequences. Two clusters of sequences are aligned by a simple extension of the pairwise alignment of two individual sequences. The final alignment is achieved by a series of progressive, pairwise alignments. The program is run by designating specific sequences and their amino acid
25 or nucleotide coordinates for regions of sequence comparison and by designating the program parameters. Using PILEUP, a reference sequence is compared to other test sequences to determine the percent sequence identity relationship using the following parameters: default gap weight (3.00), default gap length weight (0.10), and weighted end gaps. PILEUP can be obtained from the GCG sequence analysis software package, *e.g.*,
30 version 7.0 (Devereaux *et al.*, *Nuc. Acids Res.* 12:387-395 (1984)).

An indication that two nucleic acid sequences or polypeptides are substantially identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the antibodies raised against the polypeptide encoded by the second nucleic acid, as described below. Thus, a polypeptide is typically

substantially identical to a second polypeptide, for example, where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules or their complements hybridize to each other under stringent conditions, as described below. Yet another indication that two nucleic acid sequences are substantially identical is that the same primers can be used to amplify the sequence.

The phrase “selectively (or specifically) hybridizes to” refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent hybridization conditions when that sequence is present in a complex mixture (*e.g.*, total cellular or library DNA or RNA).

The phrase “stringent hybridization conditions” refers to conditions under which a probe will hybridize to its target subsequence, typically in a complex mixture of nucleic acid, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. An extensive guide to the hybridization of nucleic acids is found in Tijssen, *Techniques in Biochemistry and Molecular Biology--Hybridization with Nucleic Probes*, “Overview of principles of hybridization and the strategy of nucleic acid assays” (1993). Generally, stringent conditions are selected to be about 5-10° C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength pH. The T_m is the temperature (under defined ionic strength, pH, and nucleic concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m , 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30° C for short probes (*e.g.*, 10 to 50 nucleotides) and at least about 60° C for long probes (*e.g.*, greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. For selective or specific hybridization, a positive signal is at least two times background, optionally 10 times background hybridization. Exemplary stringent hybridization conditions can be as following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42°C, or, 5x SSC, 1% SDS, incubating at 65°C, with wash in 0.2x SSC, and 0.1% SDS at 65°C. Such hybridizations and wash steps can be carried out for, *e.g.*, 1, 2, 5, 10, 15, 30, 60, or more minutes.

Nucleic acids that do not hybridize to each other under stringent conditions are still substantially identical if the polypeptides which they encode are substantially identical. This occurs, for example, when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code. In such cases, the nucleic acids typically hybridize under moderately stringent hybridization conditions. Exemplary “moderately stringent hybridization conditions” include a hybridization in a buffer of 40% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 1X SSC at 45°C. Such hybridizations and wash steps can be carried out for, e.g., 1, 2, 5, 10, 15, 30, 60, or more minutes. A positive hybridization is at least twice background. Those of ordinary skill will readily recognize that alternative hybridization and wash conditions can be utilized to provide conditions of similar stringency.

“Antibody” refers to a polypeptide comprising a framework region from an immunoglobulin gene or fragments thereof that specifically binds and recognizes an antigen. The recognized immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon, and mu constant region genes, as well as the myriad immunoglobulin variable region genes. Light chains are classified as either kappa or lambda. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, which in turn define the immunoglobulin classes, IgG, IgM, IgA, IgD and IgE, respectively.

An exemplary immunoglobulin (antibody) structural unit comprises a tetramer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one “light” (about 25 kDa) and one “heavy” chain (about 50-70 kDa). The N-terminus of each chain defines a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The terms variable light chain (V_L) and variable heavy chain (V_H) refer to these light and heavy chains respectively.

Antibodies exist, e.g., as intact immunoglobulins or as a number of well-characterized fragments produced by digestion with various peptidases. Thus, for example, pepsin digests an antibody below the disulfide linkages in the hinge region to produce $F(ab)'_2$, a dimer of Fab which itself is a light chain joined to V_H - C_H1 by a disulfide bond. The $F(ab)'_2$ may be reduced under mild conditions to break the disulfide linkage in the hinge region, thereby converting the $F(ab)'_2$ dimer into an Fab' monomer. The Fab' monomer is essentially Fab with part of the hinge region (*see Fundamental Immunology* (Paul ed., 3d ed. 1993)). While various antibody fragments are defined in terms of the digestion of an intact antibody, one of skill will appreciate that such fragments may be synthesized *de novo* either chemically or by using recombinant DNA

methodology. Thus, the term antibody, as used herein, also includes antibody fragments either produced by the modification of whole antibodies, or those synthesized *de novo* using recombinant DNA methodologies (e.g., single chain Fv) or those identified using phage display libraries (see, e.g., McCafferty *et al.*, *Nature* 348:552-554 (1990)).

5 For preparation of monoclonal or polyclonal antibodies, any technique known in the art can be used (see, e.g., Kohler & Milstein, *Nature* 256:495-497 (1975); Kozbor *et al.*, *Immunology Today* 4: 72 (1983); Cole *et al.*, pp. 77-96 in *Monoclonal Antibodies and Cancer Therapy* (1985)). Techniques for the production of single chain antibodies (U.S. Patent 4,946,778) can be adapted to produce antibodies to polypeptides
10 of this invention. Also, transgenic mice, or other organisms such as other mammals, may be used to express humanized antibodies. Alternatively, phage display technology can be used to identify antibodies and heteromeric Fab fragments that specifically bind to selected antigens (see, e.g., McCafferty *et al.*, *Nature* 348:552-554 (1990); Marks *et al.*, *Biotechnology* 10:779-783 (1992)).

15 A “chimeric antibody” is an antibody molecule in which (a) the constant region, or a portion thereof, is altered, replaced or exchanged so that the antigen binding site (variable region) is linked to a constant region of a different or altered class, effector function and/or species, or an entirely different molecule which confers new properties to the chimeric antibody, e.g., an enzyme, toxin, hormone, growth factor, drug, etc.; or (b)
20 the variable region, or a portion thereof, is altered, replaced or exchanged with a variable region having a different or altered antigen specificity.

An “anti-T2R” antibody is an antibody or antibody fragment that specifically binds a polypeptide encoded by a T2R gene, cDNA, or a subsequence thereof.

25 The term “immunoassay” is an assay that uses an antibody to specifically bind an antigen. The immunoassay is characterized by the use of specific binding properties of a particular antibody to isolate, target, and/or quantify the antigen.

The phrase “specifically (or selectively) binds” to an antibody or “specifically (or selectively) immunoreactive with,” when referring to a protein or
30 peptide, refers to a binding reaction that is determinative of the presence of the protein in a heterogeneous population of proteins and other biologics. Thus, under designated immunoassay conditions, the specified antibodies bind to a particular protein at least two times the background and do not substantially bind in a significant amount to other proteins present in the sample. Specific binding to an antibody under such conditions

may require an antibody that is selected for its specificity for a particular protein. For example, polyclonal antibodies raised to a T2R family member from specific species such as rat, mouse, or human can be selected to obtain only those polyclonal antibodies that are specifically immunoreactive with the T2R protein or an immunogenic portion thereof and not with other proteins, except for orthologs or polymorphic variants and alleles of the T2R protein. This selection may be achieved by subtracting out antibodies that cross-react with T2R molecules from other species or other T2R molecules. Antibodies can also be selected that recognize only T2R GPCR family members but not GPCRs from other families. A variety of immunoassay formats may be used to select antibodies specifically immunoreactive with a particular protein. For example, solid-phase ELISA immunoassays are routinely used to select antibodies specifically immunoreactive with a protein (*see, e.g., Harlow & Lane, Antibodies, A Laboratory Manual* (1988), for a description of immunoassay formats and conditions that can be used to determine specific immunoreactivity). Typically a specific or selective reaction will be at least twice background signal or noise and more typically more than 10 to 100 times background.

In one embodiment, immunogenic domains corresponding to SEQ ID NOs:166-171 can be used to raise antibodies that specifically bind to polypeptides of the T2R family.

The phrase “selectively associates with” refers to the ability of a nucleic acid to “selectively hybridize” with another as defined above, or the ability of an antibody to “selectively (or specifically) bind to a protein, as defined above.

By “host cell” is meant a cell that contains an expression vector and supports the replication or expression of the expression vector. Host cells may be prokaryotic cells such as *E. coli*, or eukaryotic cells such as yeast, insect, amphibian, or mammalian cells such as CHO, HeLa, HEK-293, and the like, *e.g.,* cultured cells, explants, and cells *in vivo*.

III. Isolation of nucleic acids encoding T2R family members

A. General recombinant DNA methods

This invention relies on routine techniques in the field of recombinant genetics. Basic texts disclosing the general methods of use in this invention include Sambrook *et al., Molecular Cloning, A Laboratory Manual* (2nd ed. 1989); Kriegler,

Gene Transfer and Expression: A Laboratory Manual (1990); and *Current Protocols in Molecular Biology* (Ausubel *et al.*, eds., 1994)).

For nucleic acids, sizes are given in either kilobases (kb) or base pairs (bp). These are estimates derived from agarose or acrylamide gel electrophoresis, from sequenced nucleic acids, or from published DNA sequences. For proteins, sizes are given in kilodaltons (kDa) or amino acid residue numbers. Proteins sizes are estimated from gel electrophoresis, from sequenced proteins, from derived amino acid sequences, or from published protein sequences.

Oligonucleotides that are not commercially available can be chemically synthesized according to the solid phase phosphoramidite triester method first described by Beaucage & Caruthers, *Tetrahedron Letts.* 22:1859-1862 (1981), using an automated synthesizer, as described in Van Devanter *et al.*, *Nucleic Acids Res.* 12:6159-6168 (1984). Purification of oligonucleotides is by either native acrylamide gel electrophoresis or by anion-exchange HPLC as described in Pearson & Reanier, *J. Chrom.* 255:137-149 (1983).

The sequence of the cloned genes and synthetic oligonucleotides can be verified after cloning using, *e.g.*, the chain termination method for sequencing double-stranded templates of Wallace *et al.*, *Gene* 16:21-26 (1981).

B. Cloning methods for the isolation of nucleotide sequences encoding T2R family members

In general, the nucleic acid sequences encoding T2R family members and related nucleic acid sequence homologs are cloned from cDNA and genomic DNA libraries by hybridization with probes, or isolated using amplification techniques with oligonucleotide primers. For example, T2R sequences are typically isolated from mammalian nucleic acid (genomic or cDNA) libraries by hybridizing with a nucleic acid probe, the sequence of which can be derived from SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID

NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, or SEQ ID NO:165. A suitable tissue from which RNA and cDNA for T2R family members can be isolated is tongue tissue, optionally taste bud tissues or individual taste cells.

Amplification techniques using primers can also be used to amplify and isolate T2R sequences from DNA or RNA. For example, degenerate primers encoding the following amino acid sequences can be used to amplify a sequence of a T2R gene: SEQ ID NOS: 166, 167, 168, 169, 170, or 171 (*see, e.g., Dieffenbach & Dveksler, PCR Primer: A Laboratory Manual* (1995)). These primers can be used, *e.g.*, to amplify either the full length sequence or a probe of one to several hundred nucleotides, which is then used to screen a mammalian library for full-length T2R clones. As described above, such primers can be used to isolate a full length sequence, or a probe which can then be used to isolated a full length sequence, *e.g.*, from a library.

Nucleic acids encoding T2R can also be isolated from expression libraries using antibodies as probes. Such polyclonal or monoclonal antibodies can be raised using the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID

NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, or SEQ ID NO:164.

Polymorphic variants, alleles, and interspecies homologs that are substantially identical to a T2R family member can be isolated using T2R nucleic acid probes, and oligonucleotides under stringent hybridization conditions, by screening libraries. Alternatively, expression libraries can be used to clone T2R family members and T2R family member polymorphic variants, alleles, and interspecies homologs, by detecting expressed homologs immunologically with antisera or purified antibodies made against a T2R polypeptide, which also recognize and selectively bind to the T2R homolog.

To make a cDNA library, one should choose a source that is rich in T2R mRNA, *e.g.*, tongue tissue, or isolated taste buds. The mRNA is then made into cDNA using reverse transcriptase, ligated into a recombinant vector, and transfected into a recombinant host for propagation, screening and cloning. Methods for making and screening cDNA libraries are well known (*see, e.g.*, Gubler & Hoffman, *Gene* 25:263-269 (1983); Sambrook *et al.*, *supra*; Ausubel *et al.*, *supra*).

For a genomic library, the DNA is extracted from the tissue and either mechanically sheared or enzymatically digested to yield fragments of about 12-20 kb. The fragments are then separated by gradient centrifugation from undesired sizes and are constructed in bacteriophage lambda vectors. These vectors and phage are packaged *in vitro*. Recombinant phage are analyzed by plaque hybridization as described in Benton & Davis, *Science* 196:180-182 (1977). Colony hybridization is carried out as generally described in Grunstein *et al.*, *Proc. Natl. Acad. Sci. USA.*, 72:3961-3965 (1975).

An alternative method of isolating T2R nucleic acid and its homologs combines the use of synthetic oligonucleotide primers and amplification of an RNA or DNA template (*see* U.S. Patents 4,683,195 and 4,683,202; *PCR Protocols: A Guide to Methods and Applications* (Innis *et al.*, eds, 1990)). Methods such as polymerase chain reaction (PCR) and ligase chain reaction (LCR) can be used to amplify nucleic acid sequences of T2R genes directly from mRNA, from cDNA, from genomic libraries or cDNA libraries. Degenerate oligonucleotides can be designed to amplify T2R family

member homologs using the sequences provided herein. Restriction endonuclease sites can be incorporated into the primers. Polymerase chain reaction or other *in vitro* amplification methods may also be useful, for example, to clone nucleic acid sequences that code for proteins to be expressed, to make nucleic acids to use as probes for detecting the presence of T2R-encoding mRNA in physiological samples, for nucleic acid sequencing, or for other purposes. Genes amplified by the PCR reaction can be purified from agarose gels and cloned into an appropriate vector.

Gene expression of T2R family members can also be analyzed by techniques known in the art, *e.g.*, reverse transcription and amplification of mRNA, isolation of total RNA or poly A⁺ RNA, northern blotting, dot blotting, *in situ* hybridization, RNase protection, probing DNA microchip arrays, and the like. In one embodiment, high density oligonucleotide analysis technology (*e.g.*, GeneChip™) is used to identify homologs and polymorphic variants of the GPCRs of the invention. In the case where the homologs being identified are linked to a known disease, they can be used with GeneChip™ as a diagnostic tool in detecting the disease in a biological sample, *see, e.g.*, Gunthand *et al.*, *AIDS Res. Hum. Retroviruses* 14: 869-876 (1998); Kozal *et al.*, *Nat. Med.* 2:753-759 (1996); Matson *et al.*, *Anal. Biochem.* 224:110-106 (1995); Lockhart *et al.*, *Nat. Biotechnol.* 14:1675-1680 (1996); Gingeras *et al.*, *Genome Res.* 8:435-448 (1998); Hacia *et al.*, *Nucleic Acids Res.* 26:3865-3866 (1998).

Synthetic oligonucleotides can be used to construct recombinant T2R genes for use as probes or for expression of protein. This method is performed using a series of overlapping oligonucleotides usually 40- 120 bp in length, representing both the sense and nonsense strands of the gene. These DNA fragments are then annealed, ligated and cloned. Alternatively, amplification techniques can be used with precise primers to amplify a specific subsequence of the T2R nucleic acid. The specific subsequence is then ligated into an expression vector.

The nucleic acid encoding a T2R gene is typically cloned into intermediate vectors before transformation into prokaryotic or eukaryotic cells for replication and/or expression. These intermediate vectors are typically prokaryote vectors, *e.g.*, plasmids, or shuttle vectors.

Optionally, nucleic acids encoding chimeric proteins comprising a T2R polypeptide or domains thereof can be made according to standard techniques. For example, a domain such as a ligand binding domain (*e.g.*, an extracellular domain alone,

an extracellular domain plus a transmembrane region, or a transmembrane region alone), an extracellular domain, a transmembrane domain (e.g., one comprising up to seven transmembrane regions and corresponding extracellular and cytosolic loops), the transmembrane domain and a cytoplasmic domain, an active site, a subunit association region, *etc.*, can be covalently linked to a heterologous protein. For example, an extracellular domain can be linked to a heterologous GPCR transmembrane domain, or a heterologous GPCR extracellular domain can be linked to a transmembrane domain. Other heterologous proteins of choice include, e.g., green fluorescent protein, β -gal, glutamate receptor, and the rhodopsin presequence.

C. Expression in prokaryotes and eukaryotes

To obtain high level expression of a cloned gene or nucleic acid, such as those cDNAs encoding a T2R family member, one typically subclones the T2R sequence into an expression vector that contains a strong promoter to direct transcription, a transcription/translation terminator, and if for a nucleic acid encoding a protein, a ribosome binding site for translational initiation. Suitable bacterial promoters are well known in the art and described, e.g., in Sambrook *et al.* and Ausubel *et al.* Bacterial expression systems for expressing the T2R protein are available in, e.g., *E. coli*, *Bacillus sp.*, and *Salmonella* (Palva *et al.*, *Gene* 22:229-235 (1983); Mosbach *et al.*, *Nature* 302:543-545 (1983). Kits for such expression systems are commercially available. Eukaryotic expression systems for mammalian cells, yeast, and insect cells are well known in the art and are also commercially available. In one embodiment, the eukaryotic expression vector is an adenoviral vector, an adeno-associated vector, or a retroviral vector.

The promoter used to direct expression of a heterologous nucleic acid depends on the particular application. The promoter is optionally positioned about the same distance from the heterologous transcription start site as it is from the transcription start site in its natural setting. As is known in the art, however, some variation in this distance can be accommodated without loss of promoter function.

In addition to the promoter, the expression vector typically contains a transcription unit or expression cassette that contains all the additional elements required for the expression of the T2R-encoding nucleic acid in host cells. A typical expression cassette thus contains a promoter operably linked to the nucleic acid sequence encoding a

T2R and signals required for efficient polyadenylation of the transcript, ribosome binding sites, and translation termination. The nucleic acid sequence encoding a T2R may typically be linked to a cleavable signal peptide sequence to promote secretion of the encoded protein by the transformed cell. Such signal peptides would include, among
5 others, the signal peptides from tissue plasminogen activator, insulin, and neuron growth factor, and juvenile hormone esterase of *Heliothis virescens*. Additional elements of the cassette may include enhancers and, if genomic DNA is used as the structural gene, introns with functional splice donor and acceptor sites.

In addition to a promoter sequence, the expression cassette should also
10 contain a transcription termination region downstream of the structural gene to provide for efficient termination. The termination region may be obtained from the same gene as the promoter sequence or may be obtained from different genes.

The particular expression vector used to transport the genetic information into the cell is not particularly critical. Any of the conventional vectors used for
15 expression in eukaryotic or prokaryotic cells may be used. Standard bacterial expression vectors include plasmids such as pBR322 based plasmids, pSKF, pET23D, and fusion expression systems such as GST and LacZ. Epitope tags can also be added to recombinant proteins to provide convenient methods of isolation, *e.g.*, c-myc.

Expression vectors containing regulatory elements from eukaryotic viruses
20 are typically used in eukaryotic expression vectors, *e.g.*, SV40 vectors, papilloma virus vectors, and vectors derived from Epstein-Barr virus. Other exemplary eukaryotic vectors include pMSG, pAV009/A⁺, pMTO10/A⁺, pMAMneo-5, baculovirus pDSVE, and any other vector allowing expression of proteins under the direction of the SV40 early promoter, SV40 later promoter, metallothionein promoter, murine mammary tumor
25 virus promoter, Rous sarcoma virus promoter, polyhedrin promoter, or other promoters shown effective for expression in eukaryotic cells.

Some expression systems have markers that provide gene amplification such as neomycin, hymidine kinase, hygromycin B phosphotransferase, and dihydrofolate reductase. Alternatively, high yield expression systems not involving gene amplification
30 are also suitable, such as using a baculovirus vector in insect cells, with a sequence encoding a T2R family member under the direction of the polyhedrin promoter or other strong baculovirus promoters.

The elements that are typically included in expression vectors also include a replicon that functions in *E. coli*, a gene encoding antibiotic resistance to permit

selection of bacteria that harbor recombinant plasmids, and unique restriction sites in nonessential regions of the plasmid to allow insertion of eukaryotic sequences. The particular antibiotic resistance gene chosen is not critical, any of the many resistance genes known in the art are suitable. The prokaryotic sequences are optionally chosen
5 such that they do not interfere with the replication of the DNA in eukaryotic cells, if necessary.

Standard transfection methods are used to produce bacterial, mammalian, yeast or insect cell lines that express large quantities of a T2R protein, which are then purified using standard techniques (*see, e.g., Colley et al., J. Biol. Chem.* 264:17619-
10 17622 (1989); *Guide to Protein Purification, in Methods in Enzymology*, vol. 182 (Deutscher, ed., 1990)). Transformation of eukaryotic and prokaryotic cells are performed according to standard techniques (*see, e.g., Morrison, J. Bact.* 132:349-351 (1977); Clark-Curtiss & Curtiss, *Methods in Enzymology* 101:347-362 (Wu *et al.*, eds, 1983).

15 Any of the well known procedures for introducing foreign nucleotide sequences into host cells may be used. These include the use of calcium phosphate transfection, polybrene, protoplast fusion, electroporation, liposomes, microinjection, plasma vectors, viral vectors and any of the other well known methods for introducing cloned genomic DNA, cDNA, synthetic DNA or other foreign genetic material into a host
20 cell (*see, e.g., Sambrook et al., supra*). It is only necessary that the particular genetic engineering procedure used be capable of successfully introducing at least one gene into the host cell capable of expressing a T2R gene.

In one preferred embodiment, a polynucleotide encoding a T2R is operably linked to a EF-1 α promoter, *e.g.*, using a pEAK10 mammalian expression
25 vector (Edge Biosystems, MD) is used. Such vectors can be introduced into cells, *e.g.*, HEK-293 cells using any standard method, such as transfection using LipofectAMINE (Lifetechnologies).

After the expression vector is introduced into the cells, the transfected cells are cultured under conditions favoring expression of the T2R family member, which is
30 recovered from the culture using standard techniques identified below.

IV. Purification of T2R polypeptides

Either naturally occurring or recombinant T2R polypeptides can be purified for use in functional assays. Optionally, recombinant T2R polypeptides are purified. Naturally occurring T2R polypeptides are purified, *e.g.*, from mammalian tissue
5 such as tongue tissue, and any other source of a T2R homolog. Recombinant T2R polypeptides are purified from any suitable bacterial or eukaryotic expression system, *e.g.*, CHO cells or insect cells.

T2R proteins may be purified to substantial purity by standard techniques, including selective precipitation with such substances as ammonium sulfate; column
10 chromatography, immunopurification methods, and others (*see, e.g.*, Scopes, *Protein Purification: Principles and Practice* (1982); U.S. Patent No. 4,673,641; Ausubel *et al.*, *supra*; and Sambrook *et al.*, *supra*).

A number of procedures can be employed when recombinant T2R family members are being purified. For example, proteins having established molecular
15 adhesion properties can be reversibly fused to the T2R polypeptide. With the appropriate ligand, a T2R can be selectively adsorbed to a purification column and then freed from the column in a relatively pure form. The fused protein is then removed by enzymatic activity. Finally T2R proteins can be purified using immunoaffinity columns.

20 A. Purification of T2R protein from recombinant cells

Recombinant proteins are expressed by transformed bacteria or eukaryotic cells such as CHO cells or insect cells in large amounts, typically after promoter induction; but expression can be constitutive. Promoter induction with IPTG is a one
example of an inducible promoter system. Cells are grown according to standard
25 procedures in the art. Fresh or frozen cells are used for isolation of protein.

Proteins expressed in bacteria may form insoluble aggregates ("inclusion bodies"). Several protocols are suitable for purification of T2R inclusion bodies. For example, purification of inclusion bodies typically involves the extraction, separation and/or purification of inclusion bodies by disruption of bacterial cells, *e.g.*, by incubation
30 in a buffer of 50 mM TRIS/HCL pH 7.5, 50 mM NaCl, 5 mM MgCl₂, 1 mM DTT, 0.1 mM ATP, and 1 mM PMSF. The cell suspension can be lysed using 2-3 passages through a French Press, homogenized using a Polytron (Brinkman Instruments) or sonicated on ice. Alternate methods of lysing bacteria are apparent to those of skill in the art (*see, e.g.*, Sambrook *et al.*, *supra*; Ausubel *et al.*, *supra*).

0054033-023000

If necessary, the inclusion bodies are solubilized, and the lysed cell suspension is typically centrifuged to remove unwanted insoluble matter. Proteins that formed the inclusion bodies may be renatured by dilution or dialysis with a compatible buffer. Suitable solvents include, but are not limited to urea (from about 4 M to about 8 M), formamide (at least about 80%, volume/volume basis), and guanidine hydrochloride (from about 4 M to about 8 M). Some solvents which are capable of solubilizing aggregate-forming proteins, for example SDS (sodium dodecyl sulfate), 70% formic acid, are inappropriate for use in this procedure due to the possibility of irreversible denaturation of the proteins, accompanied by a lack of immunogenicity and/or activity. Although guanidine hydrochloride and similar agents are denaturants, this denaturation is not irreversible and renaturation may occur upon removal (by dialysis, for example) or dilution of the denaturant, allowing re-formation of immunologically and/or biologically active protein. Other suitable buffers are known to those skilled in the art. T2R polypeptides are separated from other bacterial proteins by standard separation techniques, *e.g.*, with Ni-NTA agarose resin.

Alternatively, it is possible to purify T2R polypeptides from bacteria periplasm. After lysis of the bacteria, when a T2R protein is exported into the periplasm of the bacteria, the periplasmic fraction of the bacteria can be isolated by cold osmotic shock in addition to other methods known to skill in the art. To isolate recombinant proteins from the periplasm, the bacterial cells are centrifuged to form a pellet. The pellet is resuspended in a buffer containing 20% sucrose. To lyse the cells, the bacteria are centrifuged and the pellet is resuspended in ice-cold 5 mM MgSO₄ and kept in an ice bath for approximately 10 minutes. The cell suspension is centrifuged and the supernatant decanted and saved. The recombinant proteins present in the supernatant can be separated from the host proteins by standard separation techniques well known to those of skill in the art.

B. Standard protein separation techniques for purifying T2R polypeptides

Solubility fractionation

Often as an initial step, particularly if the protein mixture is complex, an initial salt fractionation can separate many of the unwanted host cell proteins (or proteins derived from the cell culture media) from the recombinant protein of interest. The preferred salt is ammonium sulfate. Ammonium sulfate precipitates proteins by effectively reducing the amount of water in the protein mixture. Proteins then precipitate

on the basis of their solubility. The more hydrophobic a protein is, the more likely it is to precipitate at lower ammonium sulfate concentrations. A typical protocol includes adding saturated ammonium sulfate to a protein solution so that the resultant ammonium sulfate concentration is between 20-30%. This concentration will precipitate the most hydrophobic of proteins. The precipitate is then discarded (unless the protein of interest is hydrophobic) and ammonium sulfate is added to the supernatant to a concentration known to precipitate the protein of interest. The precipitate is then solubilized in buffer and the excess salt removed if necessary, either through dialysis or diafiltration. Other methods that rely on solubility of proteins, such as cold ethanol precipitation, are well known to those of skill in the art and can be used to fractionate complex protein mixtures.

Size differential filtration

The molecular weight of a T2R protein can be used to isolate it from proteins of greater and lesser size using ultrafiltration through membranes of different pore size (for example, Amicon or Millipore membranes). As a first step, the protein mixture is ultrafiltered through a membrane with a pore size that has a lower molecular weight cut-off than the molecular weight of the protein of interest. The retentate of the ultrafiltration is then ultrafiltered against a membrane with a molecular cut off greater than the molecular weight of the protein of interest. The recombinant protein will pass through the membrane into the filtrate. The filtrate can then be chromatographed as described below.

Column chromatography

T2R proteins can also be separated from other proteins on the basis of its size, net surface charge, hydrophobicity, and affinity for ligands. In addition, antibodies raised against proteins can be conjugated to column matrices and the proteins immunopurified. All of these methods are well known in the art. It will be apparent to one of skill that chromatographic techniques can be performed at any scale and using equipment from many different manufacturers (*e.g.*, Pharmacia Biotech).

30

V. Immunological detection of T2R polypeptides

In addition to the detection of T2R genes and gene expression using nucleic acid hybridization technology, one can also use immunoassays to detect T2R, *e.g.*, to identify taste receptor cells, especially bitter taste receptor cells, and variants of

T2R family members. Immunoassays can be used to qualitatively or quantitatively analyze the T2R. A general overview of the applicable technology can be found in Harlow & Lane, *Antibodies: A Laboratory Manual* (1988).

5 *A. Antibodies to T2R family members*

Methods of producing polyclonal and monoclonal antibodies that react specifically with a T2R family member are known to those of skill in the art (*see, e.g.,* Coligan, *Current Protocols in Immunology* (1991); Harlow & Lane, *supra*; Goding, *Monoclonal Antibodies: Principles and Practice* (2d ed. 1986); and Kohler & Milstein, *Nature* 256:495-497 (1975). Such techniques include antibody preparation by selection of antibodies from libraries of recombinant antibodies in phage or similar vectors, as well as preparation of polyclonal and monoclonal antibodies by immunizing rabbits or mice (*see, e.g.,* Huse *et al.*, *Science* 246:1275-1281 (1989); Ward *et al.*, *Nature* 341:544-546 (1989)).

15 A number of T2R-comprising immunogens may be used to produce antibodies specifically reactive with a T2R family member. For example, a recombinant T2R protein, or an antigenic fragment thereof, is isolated as described herein. Suitable antigenic regions include, *e.g.,* the conserved motifs that are used to identify members of the T2R family, *i.e.,* SEQ ID NOS:166, 167, 168, 169, 170, and 171. Recombinant protein can be expressed in eukaryotic or prokaryotic cells as described above, and purified as generally described above. Recombinant protein is the preferred immunogen for the production of monoclonal or polyclonal antibodies. Alternatively, a synthetic peptide derived from the sequences disclosed herein and conjugated to a carrier protein can be used as an immunogen. Naturally occurring protein may also be used either in pure or impure form. The product is then injected into an animal capable of producing antibodies. Either monoclonal or polyclonal antibodies may be generated, for subsequent use in immunoassays to measure the protein.

20 Methods of production of polyclonal antibodies are known to those of skill in the art. An inbred strain of mice (*e.g.,* BALB/C mice) or rabbits is immunized with the protein using a standard adjuvant, such as Freund's adjuvant, and a standard immunization protocol. The animal's immune response to the immunogen preparation is monitored by taking test bleeds and determining the titer of reactivity to the T2R. When appropriately high titers of antibody to the immunogen are obtained, blood is collected

from the animal and antisera are prepared. Further fractionation of the antisera to enrich for antibodies reactive to the protein can be done if desired (*see* Harlow & Lane, *supra*).

Monoclonal antibodies may be obtained by various techniques familiar to those skilled in the art. Briefly, spleen cells from an animal immunized with a desired antigen are immortalized, commonly by fusion with a myeloma cell (*see* Kohler & Milstein, *Eur. J. Immunol.* 6:511-519 (1976)). Alternative methods of immortalization include transformation with Epstein Barr Virus, oncogenes, or retroviruses, or other methods well known in the art. Colonies arising from single immortalized cells are screened for production of antibodies of the desired specificity and affinity for the antigen, and yield of the monoclonal antibodies produced by such cells may be enhanced by various techniques, including injection into the peritoneal cavity of a vertebrate host. Alternatively, one may isolate DNA sequences which encode a monoclonal antibody or a binding fragment thereof by screening a DNA library from human B cells according to the general protocol outlined by Huse *et al.*, *Science* 246:1275-1281 (1989).

Monoclonal antibodies and polyclonal sera are collected and titered against the immunogen protein in an immunoassay, for example, a solid phase immunoassay with the immunogen immobilized on a solid support. Typically, polyclonal antisera with a titer of 10^4 or greater are selected and tested for their cross reactivity against non-T2R proteins, or even other T2R family members or other related proteins from other organisms, using a competitive binding immunoassay. Specific polyclonal antisera and monoclonal antibodies will usually bind with a K_d of at least about 0.1 mM, more usually at least about 1 μ M, optionally at least about 0.1 μ M or better, and optionally 0.01 μ M or better.

Once T2R family member specific antibodies are available, individual T2R proteins can be detected by a variety of immunoassay methods. For a review of immunological and immunoassay procedures, see *Basic and Clinical Immunology* (Stites & Terr eds., 7th ed. 1991). Moreover, the immunoassays of the present invention can be performed in any of several configurations, which are reviewed extensively in *Enzyme Immunoassay* (Maggio, ed., 1980); and Harlow & Lane, *supra*.

B. Immunological binding assays

T2R proteins can be detected and/or quantified using any of a number of well recognized immunological binding assays (*see, e.g.*, U.S. Patents 4,366,241; 4,376,110; 4,517,288; and 4,837,168). For a review of the general immunoassays, see

also *Methods in Cell Biology: Antibodies in Cell Biology*, volume 37 (Asai, ed. 1993);
Basic and Clinical Immunology (Stites & Terr, eds., 7th ed. 1991). Immunological
binding assays (or immunoassays) typically use an antibody that specifically binds to a
protein or antigen of choice (in this case a T2R family member or an antigenic
5 subsequence thereof). The antibody (*e.g.*, anti-T2R) may be produced by any of a
number of means well known to those of skill in the art and as described above.

Immunoassays also often use a labeling agent to specifically bind to and
label the complex formed by the antibody and antigen. The labeling agent may itself be
one of the moieties comprising the antibody/antigen complex. Thus, the labeling agent
10 may be a labeled T2R polypeptide or a labeled anti-T2R antibody. Alternatively, the
labeling agent may be a third moiety, such a secondary antibody, that specifically binds to
the antibody/T2R complex (a secondary antibody is typically specific to antibodies of the
species from which the first antibody is derived). Other proteins capable of specifically
binding immunoglobulin constant regions, such as protein A or protein G may also be
15 used as the label agent. These proteins exhibit a strong non-immunogenic reactivity with
immunoglobulin constant regions from a variety of species (*see, e.g.*, Kronval *et al.*, *J.*
Immunol. 111:1401-1406 (1973); Akerstrom *et al.*, *J. Immunol.* 135:2589-2542 (1985)).
The labeling agent can be modified with a detectable moiety, such as biotin, to which
another molecule can specifically bind, such as streptavidin. A variety of detectable
20 moieties are well known to those skilled in the art.

Throughout the assays, incubation and/or washing steps may be required
after each combination of reagents. Incubation steps can vary from about 5 seconds to
several hours, optionally from about 5 minutes to about 24 hours. However, the
incubation time will depend upon the assay format, antigen, volume of solution,
25 concentrations, and the like. Usually, the assays will be carried out at ambient
temperature, although they can be conducted over a range of temperatures, such as 10°C
to 40°C.

Non-competitive assay formats

30 Immunoassays for detecting a T2R protein in a sample may be either
competitive or noncompetitive. Noncompetitive immunoassays are assays in which the
amount of antigen is directly measured. In one preferred “sandwich” assay, for example,
the anti-T2R antibodies can be bound directly to a solid substrate on which they are

immobilized. These immobilized antibodies then capture the T2R protein present in the test sample. The T2R protein is thus immobilized is then bound by a labeling agent, such as a second T2R antibody bearing a label. Alternatively, the second antibody may lack a label, but it may, in turn, be bound by a labeled third antibody specific to antibodies of the species from which the second antibody is derived. The second or third antibody is typically modified with a detectable moiety, such as biotin, to which another molecule specifically binds, *e.g.*, streptavidin, to provide a detectable moiety.

Competitive assay formats

In competitive assays, the amount of T2R protein present in the sample is measured indirectly by measuring the amount of a known, added (exogenous) T2R protein displaced (competed away) from an anti-T2R antibody by the unknown T2R protein present in a sample. In one competitive assay, a known amount of T2R protein is added to a sample and the sample is then contacted with an antibody that specifically binds to the T2R. The amount of exogenous T2R protein bound to the antibody is inversely proportional to the concentration of T2R protein present in the sample. In a particularly preferred embodiment, the antibody is immobilized on a solid substrate. The amount of T2R protein bound to the antibody may be determined either by measuring the amount of T2R protein present in a T2R/antibody complex, or alternatively by measuring the amount of remaining uncomplexed protein. The amount of T2R protein may be detected by providing a labeled T2R molecule.

A hapten inhibition assay is another preferred competitive assay. In this assay the known T2R protein is immobilized on a solid substrate. A known amount of anti-T2R antibody is added to the sample, and the sample is then contacted with the immobilized T2R. The amount of anti-T2R antibody bound to the known immobilized T2R protein is inversely proportional to the amount of T2R protein present in the sample. Again, the amount of immobilized antibody may be detected by detecting either the immobilized fraction of antibody or the fraction of the antibody that remains in solution. Detection may be direct where the antibody is labeled or indirect by the subsequent addition of a labeled moiety that specifically binds to the antibody as described above.

Cross-reactivity determinations

Immunoassays in the competitive binding format can also be used for crossreactivity determinations. For example, a protein at least partially encoded by SEQ

ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12,
 SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ
 ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID
 NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID
 5 NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID NO:63, SEQ ID
 NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID
 NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID
 NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID NO:106, SEQ ID
 NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID
 10 NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID
 NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID
 NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID
 NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID
 NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, or SEQ
 15 ID NO:165, can be immobilized to a solid support. Proteins (*e.g.*, T2R proteins and
 homologs) are added to the assay that compete for binding of the antisera to the
 immobilized antigen. The ability of the added proteins to compete for binding of the
 antisera to the immobilized protein is compared to the ability of the T2R polypeptide
 encoded by SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10,
 20 SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ
 ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID
 NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID
 NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID
 NO:63, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID
 25 NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID
 NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID
 NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID
 NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID
 NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID
 30 NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID
 NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID
 NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID
 NO:163, or SEQ ID NO:165 to compete with itself. The percent crossreactivity for the
 above proteins is calculated, using standard calculations. Those antisera with less than

10% crossreactivity with each of the added proteins listed above are selected and pooled. The cross-reacting antibodies are optionally removed from the pooled antisera by immunoabsorption with the added considered proteins, *e.g.*, distantly related homologs. In addition, peptides comprising amino acid sequences representing conserved motifs that are used to identify members of the T2R family can be used in cross-reactivity determinations, *i.e.*, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168; SEQ ID NO:169, SEQ ID NO:170, or SEQ ID NO:171.

The immunoabsorbed and pooled antisera are then used in a competitive binding immunoassay as described above to compare a second protein, thought to be perhaps an allele or polymorphic variant of a T2R family member, to the immunogen protein (*i.e.*, T2R protein encoded by SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, or SEQ ID NO:165). In order to make this comparison, the two proteins are each assayed at a wide range of concentrations and the amount of each protein required to inhibit 50% of the binding of the antisera to the immobilized protein is determined. If the amount of the second protein required to inhibit 50% of binding is less than 10 times the amount of the protein encoded by SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID NO:63, SEQ ID

NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, or SEQ ID NO:165 that is required to inhibit 50% of binding, then the second protein is said to specifically bind to the polyclonal antibodies generated to a T2R immunogen.

Antibodies raised against SEQ ID NOs:166-171 can also be used to prepare antibodies that specifically bind only to GPCRs of the T2R family, but not to GPCRs from other families.

Polyclonal antibodies that specifically bind to a particular member of the T2R family, *e.g.*, T2R01, can be make by subtracting out cross-reactive antibodies using other T2R family members. Species-specific polyclonal antibodies can be made in a similar way. For example, antibodies specific to human T2R01 can be made by subtracting out antibodies that are cross-reactive with orthologous sequences, *e.g.*, rat T2R01 or mouse T2R19.

Other assay formats

Western blot (immunoblot) analysis is used to detect and quantify the presence of T2R protein in the sample. The technique generally comprises separating sample proteins by gel electrophoresis on the basis of molecular weight, transferring the separated proteins to a suitable solid support, (such as a nitrocellulose filter, a nylon filter, or derivatized nylon filter), and incubating the sample with the antibodies that specifically bind the T2R protein. The anti-T2R polypeptide antibodies specifically bind to the T2R polypeptide on the solid support. These antibodies may be directly labeled or alternatively may be subsequently detected using labeled antibodies (*e.g.*, labeled sheep anti-mouse antibodies) that specifically bind to the anti-T2R antibodies.

Other assay formats include liposome immunoassays (LIA), which use liposomes designed to bind specific molecules (*e.g.*, antibodies) and release encapsulated

reagents or markers. The released chemicals are then detected according to standard techniques (see Monroe *et al.*, *Amer. Clin. Prod. Rev.* 5:34-41 (1986)).

Reduction of non-specific binding

5 One of skill in the art will appreciate that it is often desirable to minimize non-specific binding in immunoassays. Particularly, where the assay involves an antigen or antibody immobilized on a solid substrate it is desirable to minimize the amount of non-specific binding to the substrate. Means of reducing such non-specific binding are well known to those of skill in the art. Typically, this technique involves coating the
10 substrate with a proteinaceous composition. In particular, protein compositions such as bovine serum albumin (BSA), nonfat powdered milk, and gelatin are widely used with powdered milk being most preferred.

Labels

15 The particular label or detectable group used in the assay is not a critical aspect of the invention, as long as it does not significantly interfere with the specific binding of the antibody used in the assay. The detectable group can be any material having a detectable physical or chemical property. Such detectable labels have been well-developed in the field of immunoassays and, in general, most any label useful in such
20 methods can be applied to the present invention. Thus, a label is any composition detectable by spectroscopic, photochemical, biochemical, immunochemical, electrical, optical or chemical means. Useful labels in the present invention include magnetic beads (*e.g.*, DYNABEADSTM), fluorescent dyes (*e.g.*, fluorescein isothiocyanate, Texas red, rhodamine, and the like), radiolabels (*e.g.*, ³H, ¹²⁵I, ³⁵S, ¹⁴C, or ³²P), enzymes (*e.g.*, horse
25 radish peroxidase, alkaline phosphatase and others commonly used in an ELISA), and colorimetric labels such as colloidal gold or colored glass or plastic beads (*e.g.*, polystyrene, polypropylene, latex, *etc.*).

 The label may be coupled directly or indirectly to the desired component of the assay according to methods well known in the art. As indicated above, a wide
30 variety of labels may be used, with the choice of label depending on sensitivity required, ease of conjugation with the compound, stability requirements, available instrumentation, and disposal provisions.

 Non-radioactive labels are often attached by indirect means. Generally, a ligand molecule (*e.g.*, biotin) is covalently bound to the molecule. The ligand then binds

to another molecules (*e.g.*, streptavidin) molecule, which is either inherently detectable or covalently bound to a signal system, such as a detectable enzyme, a fluorescent compound, or a chemiluminescent compound. The ligands and their targets can be used in any suitable combination with antibodies that recognize a T2R protein, or secondary antibodies that recognize anti-T2R.

The molecules can also be conjugated directly to signal generating compounds, *e.g.*, by conjugation with an enzyme or fluorophore. Enzymes of interest as labels will primarily be hydrolases, particularly phosphatases, esterases and glycosidases, or oxidotases, particularly peroxidases. Fluorescent compounds include fluorescein and its derivatives, rhodamine and its derivatives, dansyl, umbelliferone, *etc.* Chemiluminescent compounds include luciferin, and 2,3-dihydrophthalazinediones, *e.g.*, luminol. For a review of various labeling or signal producing systems that may be used, see U.S. Patent No. 4,391,904.

Means of detecting labels are well known to those of skill in the art. Thus, for example, where the label is a radioactive label, means for detection include a scintillation counter or photographic film as in autoradiography. Where the label is a fluorescent label, it may be detected by exciting the fluorochrome with the appropriate wavelength of light and detecting the resulting fluorescence. The fluorescence may be detected visually, by means of photographic film, by the use of electronic detectors such as charge coupled devices (CCDs) or photomultipliers and the like. Similarly, enzymatic labels may be detected by providing the appropriate substrates for the enzyme and detecting the resulting reaction product. Finally simple colorimetric labels may be detected simply by observing the color associated with the label. Thus, in various dipstick assays, conjugated gold often appears pink, while various conjugated beads appear the color of the bead.

Some assay formats do not require the use of labeled components. For instance, agglutination assays can be used to detect the presence of the target antibodies. In this case, antigen-coated particles are agglutinated by samples comprising the target antibodies. In this format, none of the components need be labeled and the presence of the target antibody is detected by simple visual inspection.

VI. Assays for modulators of T2R family members

A. Assays for T2R protein activity

T2R family members and their alleles and polymorphic variants are G-protein coupled receptors that participate in taste transduction, *e.g.*, bitter taste

- 5 transduction. The activity of T2R polypeptides can be assessed using a variety of *in vitro* and *in vivo* assays to determine functional, chemical, and physical effects, *e.g.*, measuring ligand binding (*e.g.*, radioactive ligand binding), second messengers (*e.g.*, cAMP, cGMP, IP₃, DAG, or Ca²⁺), ion flux, phosphorylation levels, transcription levels, neurotransmitter levels, and the like. Furthermore, such assays can be used to test for inhibitors and
- 10 activators of T2R family members. Modulators can also be genetically altered versions of T2R receptors. Such modulators of taste transduction activity are useful for customizing taste, for example to modify the detection of bitter tastes.

- The T2R protein of the assay will typically be selected from a polypeptide having a sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ
- 15 ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID
- 20 NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID
- 25 NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID
- 30 NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, or SEQ ID NO:164 or conservatively modified variant thereof.

Alternatively, the T2R protein of the assay will be derived from a eukaryote and include an amino acid subsequence having amino acid sequence identity to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, or SEQ ID NO:164. Generally, the amino acid sequence identity will be at least 60%, optionally at least 70% to 85%, optionally at least 90-95%. Optionally, the polypeptide of the assays will comprise a domain of a T2R protein, such as an extracellular domain, transmembrane region, transmembrane domain, cytoplasmic domain, ligand binding domain, subunit association domain, active site, and the like. Either the T2R protein or a domain thereof can be covalently linked to a heterologous protein to create a chimeric protein used in the assays described herein.

Modulators of T2R receptor activity are tested using T2R polypeptides as described above, either recombinant or naturally occurring. The protein can be isolated, expressed in a cell, expressed in a membrane derived from a cell, expressed in tissue or in an animal, either recombinant or naturally occurring. For example, tongue slices, dissociated cells from a tongue, transformed cells, or membranes can be used. Modulation is tested using one of the *in vitro* or *in vivo* assays described herein. Taste transduction can also be examined *in vitro* with soluble or solid state reactions, using a full-length

T2R-GPCR or a chimeric molecule such as an extracellular domain or transmembrane region, or combination thereof, of a T2R receptor covalently linked to a heterologous signal transduction domain, or a heterologous extracellular domain and/or transmembrane region covalently linked to the transmembrane and/or cytoplasmic domain of a T2R receptor. Furthermore, ligand-binding domains of the protein of interest can be used *in vitro* in soluble or solid state reactions to assay for ligand binding. In numerous embodiments, a chimeric receptor will be made that comprises all or part of a T2R polypeptide as well as an additional sequence that facilitates the localization of the T2R to the membrane, such as a rhodopsin, *e.g.*, an N-terminal fragment of a rhodopsin protein.

Ligand binding to a T2R protein, a domain, or chimeric protein can be tested in solution, in a bilayer membrane, attached to a solid phase, in a lipid monolayer, or in vesicles. Binding of a modulator can be tested using, *e.g.*, changes in spectroscopic characteristics (*e.g.*, fluorescence, absorbance, refractive index) hydrodynamic (*e.g.*, shape), chromatographic, or solubility properties.

Receptor-G-protein interactions can also be examined. For example, binding of the G-protein to the receptor or its release from the receptor can be examined. For example, in the absence of GTP, an activator will lead to the formation of a tight complex of a G protein (all three subunits) with the receptor. This complex can be detected in a variety of ways, as noted above. Such an assay can be modified to search for inhibitors, *e.g.*, by adding an activator to the receptor and G protein in the absence of GTP, which form a tight complex, and then screen for inhibitors by looking at dissociation of the receptor-G protein complex. In the presence of GTP, release of the alpha subunit of the G protein from the other two G protein subunits serves as a criterion of activation.

In particularly preferred embodiments, T2R-Gustducin interactions are monitored as a function of T2R receptor activation. As shown in Example IX, mouse T2R5 shows strong cycloheximide-dependent coupling with Gustducin. Such ligand dependent coupling of T2R receptors with Gustducin can be used as a marker to identify modifiers of any member of the T2R family.

An activated or inhibited G-protein will in turn alter the properties of target enzymes, channels, and other effector proteins. The classic examples are the activation of cGMP phosphodiesterase by transducin in the visual system, adenylate cyclase by the stimulatory G-protein, phospholipase C by Gq and other cognate G proteins, and modulation of diverse channels by Gi and other G proteins. Downstream

consequences can also be examined such as generation of diacyl glycerol and IP3 by phospholipase C, and in turn, for calcium mobilization by IP3.

In a preferred embodiment, a T2R polypeptide is expressed in a eukaryotic cell as a chimeric receptor with a heterologous, chaperone sequence that facilitates its maturation and targeting through the secretory pathway. In a preferred embodiment, the heterologous sequence is a rhodopsin sequence, such as an N-terminal fragment of a rhodopsin. Such chimeric T2R receptors can be expressed in any eukaryotic cell, such as HEK-293 cells. Preferably, the cells comprise a functional G protein, *e.g.*, G α 15, that is capable of coupling the chimeric receptor to an intracellular signaling pathway or to a signaling protein such as phospholipase C β . Activation of such chimeric receptors in such cells can be detected using any standard method, such as by detecting changes in intracellular calcium by detecting FURA-2 dependent fluorescence in the cell.

Activated GPCR receptors become substrates for kinases that phosphorylate the C-terminal tail of the receptor (and possibly other sites as well). Thus, activators will promote the transfer of ^{32}P from gamma-labeled GTP to the receptor, which can be assayed with a scintillation counter. The phosphorylation of the C-terminal tail will promote the binding of arrestin-like proteins and will interfere with the binding of G-proteins. The kinase/arrestin pathway plays a key role in the desensitization of many GPCR receptors. For example, compounds that modulate the duration a taste receptor stays active would be useful as a means of prolonging a desired taste or cutting off an unpleasant one. For a general review of GPCR signal transduction and methods of assaying signal transduction, *see, e.g., Methods in Enzymology*, vols. 237 and 238 (1994) and volume 96 (1983); Bourne *et al.*, *Nature* 10:349:117-27 (1991); Bourne *et al.*, *Nature* 348:125-32 (1990); Pitcher *et al.*, *Annu. Rev. Biochem.* 67:653-92 (1998).

Samples or assays that are treated with a potential T2R protein inhibitor or activator are compared to control samples without the test compound, to examine the extent of modulation. Such assays may be carried out in the presence of a bitter tastant that is known to activate the particular receptor, and modulation of the bitter-tastant-dependent activation monitored. Control samples (untreated with activators or inhibitors) are assigned a relative T2R activity value of 100. Inhibition of a T2R protein is achieved when the T2R activity value relative to the control is about 90%, optionally 50%, optionally 25-0%. Activation of a T2R protein is achieved when the T2R activity value relative to the control is 110%, optionally 150%, 200-500%, or 1000-2000%.

Changes in ion flux may be assessed by determining changes in polarization (*i.e.*, electrical potential) of the cell or membrane expressing a T2R protein. One means to determine changes in cellular polarization is by measuring changes in current (thereby measuring changes in polarization) with voltage-clamp and patch-clamp techniques, *e.g.*, the “cell-attached” mode, the “inside-out” mode, and the “whole cell” mode (*see, e.g.*, Ackerman *et al.*, *New Engl. J. Med.* 336:1575-1595 (1997)). Whole cell currents are conveniently determined using the standard methodology (*see, e.g.*, Hamil *et al.*, *Pflugers. Archiv.* 391:85 (1981)). Other known assays include: radiolabeled ion flux assays and fluorescence assays using voltage-sensitive dyes (*see, e.g.*, Vestergaard-Bogind *et al.*, *J. Membrane Biol.* 88:67-75 (1988); Gonzales & Tsien, *Chem. Biol.* 4:269-277 (1997); Daniel *et al.*, *J. Pharmacol. Meth.* 25:185-193 (1991); Holevinsky *et al.*, *J. Membrane Biology* 137:59-70 (1994)). Generally, the compounds to be tested are present in the range from 1 pM to 100 mM.

The effects of the test compounds upon the function of the polypeptides can be measured by examining any of the parameters described above. Any suitable physiological change that affects GPCR activity can be used to assess the influence of a test compound on the polypeptides of this invention. When the functional consequences are determined using intact cells or animals, one can also measure a variety of effects such as transmitter release, hormone release, transcriptional changes to both known and uncharacterized genetic markers (*e.g.*, northern blots), changes in cell metabolism such as cell growth or pH changes, and changes in intracellular second messengers such as Ca²⁺, IP3, cGMP, or cAMP.

Preferred assays for G-protein coupled receptors include cells that are loaded with ion or voltage sensitive dyes to report receptor activity. Assays for determining activity of such receptors can also use known agonists and antagonists for other G-protein coupled receptors as negative or positive controls to assess activity of tested compounds. In assays for identifying modulatory compounds (*e.g.*, agonists, antagonists), changes in the level of ions in the cytoplasm or membrane voltage will be monitored using an ion sensitive or membrane voltage fluorescent indicator, respectively. Among the ion-sensitive indicators and voltage probes that may be employed are those disclosed in the Molecular Probes 1997 Catalog. For G-protein coupled receptors, promiscuous G-proteins such as Gα15 and Gα16 can be used in the assay of choice

(Wilkie *et al.*, *Proc. Nat'l Acad. Sci. USA* 88:10049-10053 (1991)). Such promiscuous G-proteins allow coupling of a wide range of receptors.

Receptor activation typically initiates subsequent intracellular events, *e.g.*, increases in second messengers such as IP₃, which releases intracellular stores of calcium ions. Activation of some G-protein coupled receptors stimulates the formation of inositol triphosphate (IP₃) through phospholipase C-mediated hydrolysis of phosphatidylinositol (Berridge & Irvine, *Nature* 312:315-21 (1984)). IP₃ in turn stimulates the release of intracellular calcium ion stores. Thus, a change in cytoplasmic calcium ion levels, or a change in second messenger levels such as IP₃ can be used to assess G-protein coupled receptor function. Cells expressing such G-protein coupled receptors may exhibit increased cytoplasmic calcium levels as a result of contribution from both intracellular stores and via activation of ion channels, in which case it may be desirable although not necessary to conduct such assays in calcium-free buffer, optionally supplemented with a chelating agent such as EGTA, to distinguish fluorescence response resulting from calcium release from internal stores.

Other assays can involve determining the activity of receptors which, when activated, result in a change in the level of intracellular cyclic nucleotides, *e.g.*, cAMP or cGMP, by activating or inhibiting enzymes such as adenylate cyclase. There are cyclic nucleotide-gated ion channels, *e.g.*, rod photoreceptor cell channels and olfactory neuron channels that are permeable to cations upon activation by binding of cAMP or cGMP (*see, e.g.*, Altenhofen *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* 88:9868-9872 (1991) and Dhallan *et al.*, *Nature* 347:184-187 (1990)). In cases where activation of the receptor results in a decrease in cyclic nucleotide levels, it may be preferable to expose the cells to agents that increase intracellular cyclic nucleotide levels, *e.g.*, forskolin, prior to adding a receptor-activating compound to the cells in the assay. Cells for this type of assay can be made by co-transfection of a host cell with DNA encoding a cyclic nucleotide-gated ion channel, GPCR phosphatase and DNA encoding a receptor (*e.g.*, certain glutamate receptors, muscarinic acetylcholine receptors, dopamine receptors, serotonin receptors, and the like), which, when activated, causes a change in cyclic nucleotide levels in the cytoplasm.

In a preferred embodiment, T2R protein activity is measured by expressing a T2R gene in a heterologous cell with a promiscuous G-protein that links the receptor to a phospholipase C signal transduction pathway (*see Offermanns & Simon, J. Biol. Chem.* 270:15175-15180 (1995)). Optionally the cell line is HEK-293 (which does not naturally

express T2R genes) and the promiscuous G-protein is Gα15 (Offermanns & Simon, *supra*). Modulation of taste transduction is assayed by measuring changes in intracellular Ca²⁺ levels, which change in response to modulation of the T2R signal transduction pathway via administration of a molecule that associates with a T2R protein. Changes in Ca²⁺ levels are optionally measured using fluorescent Ca²⁺ indicator dyes and fluorometric imaging.

In one embodiment, the changes in intracellular cAMP or cGMP can be measured using immunoassays. The method described in Offermanns & Simon, *J. Biol. Chem.* 270:15175-15180 (1995) may be used to determine the level of cAMP. Also, the method described in Felley-Bosco *et al.*, *Am. J. Resp. Cell and Mol. Biol.* 11:159-164 (1994) may be used to determine the level of cGMP. Further, an assay kit for measuring cAMP and/or cGMP is described in U.S. Patent 4,115,538, herein incorporated by reference.

In another embodiment, phosphatidyl inositol (PI) hydrolysis can be analyzed according to U.S. Patent 5,436,128, herein incorporated by reference. Briefly, the assay involves labeling of cells with ³H-myoinositol for 48 or more hrs. The labeled cells are treated with a test compound for one hour. The treated cells are lysed and extracted in chloroform-methanol-water after which the inositol phosphates were separated by ion exchange chromatography and quantified by scintillation counting. Fold stimulation is determined by calculating the ratio of cpm in the presence of agonist to cpm in the presence of buffer control. Likewise, fold inhibition is determined by calculating the ratio of cpm in the presence of antagonist to cpm in the presence of buffer control (which may or may not contain an agonist).

In another embodiment, transcription levels can be measured to assess the effects of a test compound on signal transduction. A host cell containing a T2R protein of interest is contacted with a test compound for a sufficient time to effect any interactions, and then the level of gene expression is measured. The amount of time to effect such interactions may be empirically determined, such as by running a time course and measuring the level of transcription as a function of time. The amount of transcription may be measured by using any method known to those of skill in the art to be suitable. For example, mRNA expression of the protein of interest may be detected using northern blots or their polypeptide products may be identified using immunoassays. Alternatively, transcription based assays using reporter gene may be used as described in U.S. Patent

5,436,128, herein incorporated by reference. The reporter genes can be, *e.g.*, chloramphenicol acetyltransferase, luciferase, β -galactosidase and alkaline phosphatase. Furthermore, the protein of interest can be used as an indirect reporter via attachment to a second reporter such as green fluorescent protein (*see, e.g.*, Mistili & Spector, *Nature*
5 *Biotechnology* 15:961-964 (1997)).

The amount of transcription is then compared to the amount of transcription in either the same cell in the absence of the test compound, or it may be compared with the amount of transcription in a substantially identical cell that lacks the protein of interest. A substantially identical cell may be derived from the same cells from
10 which the recombinant cell was prepared but which had not been modified by introduction of heterologous DNA. Any difference in the amount of transcription indicates that the test compound has in some manner altered the activity of the protein of interest.

15 *B. Modulators*

The compounds tested as modulators of a T2R family member can be any small chemical compound, or a biological entity, such as a protein, sugar, nucleic acid or lipid. Alternatively, modulators can be genetically altered versions of a T2R gene. Typically, test compounds will be small chemical molecules and peptides. Essentially
20 any chemical compound can be used as a potential modulator or ligand in the assays of the invention, although most often compounds can be dissolved in aqueous or organic (especially DMSO-based) solutions are used. The assays are designed to screen large chemical libraries by automating the assay steps and providing compounds from any convenient source to assays, which are typically run in parallel (*e.g.*, in microtiter formats
25 on microtiter plates in robotic assays). It will be appreciated that there are many suppliers of chemical compounds, including Sigma (St. Louis, MO), Aldrich (St. Louis, MO), Sigma-Aldrich (St. Louis, MO), Fluka Chemika-Biochemica Analytika (Buchs, Switzerland) and the like.

In one preferred embodiment, high throughput screening methods involve
30 providing a combinatorial chemical or peptide library containing a large number of potential therapeutic compounds (potential modulator or ligand compounds). Such “combinatorial chemical libraries” or “ligand libraries” are then screened in one or more assays, as described herein, to identify those library members (particular chemical species

or subclasses) that display a desired characteristic activity. The compounds thus identified can serve as conventional "lead compounds" or can themselves be used as potential or actual therapeutics.

A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis, by combining a number of chemical "building blocks" such as reagents. For example, a linear combinatorial chemical library such as a polypeptide library is formed by combining a set of chemical building blocks (amino acids) in every possible way for a given compound length (i.e., the number of amino acids in a polypeptide compound). Millions of chemical compounds can be synthesized through such combinatorial mixing of chemical building blocks.

Preparation and screening of combinatorial chemical libraries is well known to those of skill in the art. Such combinatorial chemical libraries include, but are not limited to, peptide libraries (*see, e.g.*, U.S. Patent 5,010,175, Furka, *Int. J. Pept. Prot. Res.* 37:487-493 (1991) and Houghton *et al.*, *Nature* 354:84-88 (1991)). Other chemistries for generating chemical diversity libraries can also be used. Such chemistries include, but are not limited to: peptoids (*e.g.*, PCT Publication No. WO 91/19735), encoded peptides (*e.g.*, PCT Publication WO 93/20242), random bio-oligomers (*e.g.*, PCT Publication No. WO 92/00091), benzodiazepines (*e.g.*, U.S. Pat. No. 5,288,514), diversomers such as hydantoins, benzodiazepines and dipeptides (Hobbs *et al.*, *Proc. Nat. Acad. Sci. USA* 90:6909-6913 (1993)), vinylogous polypeptides (Hagihara *et al.*, *J. Amer. Chem. Soc.* 114:6568 (1992)), nonpeptidal peptidomimetics with glucose scaffolding (Hirschmann *et al.*, *J. Amer. Chem. Soc.* 114:9217-9218 (1992)), analogous organic syntheses of small compound libraries (Chen *et al.*, *J. Amer. Chem. Soc.* 116:2661 (1994)), oligocarbamates (Cho *et al.*, *Science* 261:1303 (1993)), and/or peptidyl phosphonates (Campbell *et al.*, *J. Org. Chem.* 59:658 (1994)), nucleic acid libraries (*see* Ausubel, Berger and Sambrook, all *supra*), peptide nucleic acid libraries (*see, e.g.*, U.S. Patent 5,539,083), antibody libraries (*see, e.g.*, Vaughn *et al.*, *Nature Biotechnology*, 14(3):309-314 (1996) and PCT/US96/10287), carbohydrate libraries (*see, e.g.*, Liang *et al.*, *Science*, 274:1520-1522 (1996) and U.S. Patent 5,593,853), small organic molecule libraries (*see, e.g.*, benzodiazepines, Baum C&EN, Jan 18, page 33 (1993); isoprenoids, U.S. Patent 5,569,588; thiazolidinones and metathiazanones, U.S. Patent 5,549,974; pyrrolidines, U.S. Patents 5,525,735 and 5,519,134; morpholino compounds, U.S. Patent 5,506,337; benzodiazepines, 5,288,514, and the like).

Devices for the preparation of combinatorial libraries are commercially available (*see, e.g.*, 357 MPS, 390 MPS, Advanced Chem Tech, Louisville KY, Symphony, Rainin, Woburn, MA, 433A Applied Biosystems, Foster City, CA, 9050 Plus, Millipore, Bedford, MA). In addition, numerous combinatorial libraries are themselves
5 commercially available (*see, e.g.*, ComGenex, Princeton, N.J., Tripos, Inc., St. Louis, MO, 3D Pharmaceuticals, Exton, PA, Martek Biosciences, Columbia, MD, etc.).

C. Solid state and soluble high throughput assays

In one embodiment the invention provide soluble assays using molecules
10 such as a domain such as ligand binding domain, an extracellular domain, a transmembrane domain (*e.g.*, one comprising seven transmembrane regions and cytosolic loops), the transmembrane domain and a cytoplasmic domain, an active site, a subunit association region, *etc.*; a domain that is covalently linked to a heterologous protein to create a chimeric molecule; a T2R protein; or a cell or tissue expressing a T2R protein,
15 either naturally occurring or recombinant. In another embodiment, the invention provides solid phase based *in vitro* assays in a high throughput format, where the domain, chimeric molecule, T2R protein, or cell or tissue expressing the T2R is attached to a solid phase substrate.

In the high throughput assays of the invention, it is possible to screen up to
20 several thousand different modulators or ligands in a single day. In particular, each well of a microtiter plate can be used to run a separate assay against a selected potential modulator, or, if concentration or incubation time effects are to be observed, every 5-10 wells can test a single modulator. Thus, a single standard microtiter plate can assay about 100 (*e.g.*, 96) modulators. If 1536 well plates are used, then a single plate can easily
25 assay from about 100- about 1500 different compounds. It is possible to assay several different plates per day; assay screens for up to about 6,000-20,000 different compounds is possible using the integrated systems of the invention. More recently, microfluidic approaches to reagent manipulation have been developed.

The molecule of interest can be bound to the solid state component,
30 directly or indirectly, via covalent or non covalent linkage, *e.g.*, via a tag. The tag can be any of a variety of components. In general, a molecule which binds the tag (a tag binder) is fixed to a solid support, and the tagged molecule of interest (*e.g.*, the taste transduction molecule of interest) is attached to the solid support by interaction of the tag and the tag binder.

A number of tags and tag binders can be used, based upon known molecular interactions well described in the literature. For example, where a tag has a natural binder, for example, biotin, protein A, or protein G, it can be used in conjunction with appropriate tag binders (avidin, streptavidin, neutravidin, the Fc region of an immunoglobulin, *etc.*) Antibodies to molecules with natural binders such as biotin are also widely available and appropriate tag binders; *see*, SIGMA Immunochemicals 1998 catalogue SIGMA, St. Louis MO).

Similarly, any haptenic or antigenic compound can be used in combination with an appropriate antibody to form a tag/tag binder pair. Thousands of specific antibodies are commercially available and many additional antibodies are described in the literature. For example, in one common configuration, the tag is a first antibody and the tag binder is a second antibody which recognizes the first antibody. In addition to antibody-antigen interactions, receptor-ligand interactions are also appropriate as tag and tag-binder pairs. For example, agonists and antagonists of cell membrane receptors (e.g., cell receptor-ligand interactions such as transferrin, c-kit, viral receptor ligands, cytokine receptors, chemokine receptors, interleukin receptors, immunoglobulin receptors and antibodies, the cadherein family, the integrin family, the selectin family, and the like; *see, e.g.*, Pigott & Power, *The Adhesion Molecule Facts Book I* (1993). Similarly, toxins and venoms, viral epitopes, hormones (e.g., opiates, steroids, *etc.*), intracellular receptors (e.g. which mediate the effects of various small ligands, including steroids, thyroid hormone, retinoids and vitamin D; peptides), drugs, lectins, sugars, nucleic acids (both linear and cyclic polymer configurations), oligosaccharides, proteins, phospholipids and antibodies can all interact with various cell receptors.

Synthetic polymers, such as polyurethanes, polyesters, polycarbonates, polyureas, polyamides, polyethyleneimines, polyarylene sulfides, polysiloxanes, polyimides, and polyacetates can also form an appropriate tag or tag binder. Many other tag/tag binder pairs are also useful in assay systems described herein, as would be apparent to one of skill upon review of this disclosure.

Common linkers such as peptides, polyethers, and the like can also serve as tags, and include polypeptide sequences, such as poly gly sequences of between about 5 and 200 amino acids. Such flexible linkers are known to persons of skill in the art. For example, poly(ethelyne glycol) linkers are available from Shearwater Polymers, Inc. Huntsville, Alabama. These linkers optionally have amide linkages, sulfhydryl linkages, or heterofunctional linkages.

Tag binders are fixed to solid substrates using any of a variety of methods currently available. Solid substrates are commonly derivatized or functionalized by exposing all or a portion of the substrate to a chemical reagent which fixes a chemical group to the surface which is reactive with a portion of the tag binder. For example,

5 groups which are suitable for attachment to a longer chain portion would include amines, hydroxyl, thiol, and carboxyl groups. Aminoalkylsilanes and hydroxyalkylsilanes can be used to functionalize a variety of surfaces, such as glass surfaces. The construction of such solid phase biopolymer arrays is well described in the literature. *See, e.g.,* Merrifield, *J. Am. Chem. Soc.* 85:2149-2154 (1963) (describing solid phase synthesis of,

10 *e.g.,* peptides); Geysen *et al.*, *J. Immun. Meth.* 102:259-274 (1987) (describing synthesis of solid phase components on pins); Frank & Doring, *Tetrahedron* 44:60316040 (1988) (describing synthesis of various peptide sequences on cellulose disks); Fodor *et al.*, *Science*, 251:767-777 (1991); Sheldon *et al.*, *Clinical Chemistry* 39(4):718-719 (1993); and Kozal *et al.*, *Nature Medicine* 2(7):753759 (1996) (all describing arrays of

15 biopolymers fixed to solid substrates). Non-chemical approaches for fixing tag binders to substrates include other common methods, such as heat, cross-linking by UV radiation, and the like.

D. Computer-based assays

20 Yet another assay for compounds that modulate T2R protein activity involves computer assisted drug design, in which a computer system is used to generate a three-dimensional structure of a T2R protein based on the structural information encoded by its amino acid sequence. The input amino acid sequence interacts directly and actively with a preestablished algorithm in a computer program to yield secondary, tertiary, and

25 quaternary structural models of the protein. The models of the protein structure are then examined to identify regions of the structure that have the ability to bind, *e.g.*, ligands. These regions are then used to identify ligands that bind to the protein.

The three-dimensional structural model of the protein is generated by entering protein amino acid sequences of at least 10 amino acid residues or corresponding

30 nucleic acid sequences encoding a T2R polypeptide into the computer system. The nucleotide sequence encoding the polypeptide, or the amino acid sequence thereof, can be any of SEQ ID NO:1-165, and conservatively modified versions thereof. The amino acid sequence represents the primary sequence or subsequence of the protein, which encodes the structural information of the protein. At least 10 residues of the amino acid sequence

(or a nucleotide sequence encoding 10 amino acids) are entered into the computer system from computer keyboards, computer readable substrates that include, but are not limited to, electronic storage media (*e.g.*, magnetic diskettes, tapes, cartridges, and chips), optical media (*e.g.*, CD ROM), information distributed by internet sites, and by RAM. The
5 three-dimensional structural model of the protein is then generated by the interaction of the amino acid sequence and the computer system, using software known to those of skill in the art.

The amino acid sequence represents a primary structure that encodes the information necessary to form the secondary, tertiary and quaternary structure of the
10 protein of interest. The software looks at certain parameters encoded by the primary sequence to generate the structural model. These parameters are referred to as “energy terms,” and primarily include electrostatic potentials, hydrophobic potentials, solvent accessible surfaces, and hydrogen bonding. Secondary energy terms include van der Waals potentials. Biological molecules form the structures that minimize the energy
15 terms in a cumulative fashion. The computer program is therefore using these terms encoded by the primary structure or amino acid sequence to create the secondary structural model.

The tertiary structure of the protein encoded by the secondary structure is then formed on the basis of the energy terms of the secondary structure. The user at this
20 point can enter additional variables such as whether the protein is membrane bound or soluble, its location in the body, and its cellular location, *e.g.*, cytoplasmic, surface, or nuclear. These variables along with the energy terms of the secondary structure are used to form the model of the tertiary structure. In modeling the tertiary structure, the computer program matches hydrophobic faces of secondary structure with like, and
25 hydrophilic faces of secondary structure with like.

Once the structure has been generated, potential ligand binding regions are identified by the computer system. Three-dimensional structures for potential ligands are generated by entering amino acid or nucleotide sequences or chemical formulas of compounds, as described above. The three-dimensional structure of the potential ligand
30 is then compared to that of the T2R protein to identify ligands that bind to the protein. Binding affinity between the protein and ligands is determined using energy terms to determine which ligands have an enhanced probability of binding to the protein.

Computer systems are also used to screen for mutations, polymorphic variants, alleles and interspecies homologs of T2R genes. Such mutations can be

associated with disease states or genetic traits. As described above, GeneChip™ and related technology can also be used to screen for mutations, polymorphic variants, alleles and interspecies homologs. Once the variants are identified, diagnostic assays can be used to identify patients having such mutated genes. Identification of the mutated T2R genes involves receiving input of a first nucleic acid or amino acid sequence of a T2R gene, *e.g.*, any of SEQ ID NO:1-165, or conservatively modified versions thereof. The sequence is entered into the computer system as described above. The first nucleic acid or amino acid sequence is then compared to a second nucleic acid or amino acid sequence that has substantial identity to the first sequence. The second sequence is entered into the computer system in the manner described above. Once the first and second sequences are compared, nucleotide or amino acid differences between the sequences are identified. Such sequences can represent allelic differences in various T2R genes, and mutations associated with disease states and genetic traits.

IX. Administration and pharmaceutical compositions

Taste modulators can be administered directly to the mammalian subject for modulation of taste, *e.g.*, modulation of bitter taste, *in vivo*. Administration is by any of the routes normally used for introducing a modulator compound into ultimate contact with the tissue to be treated, optionally the tongue or mouth. The taste modulators are administered in any suitable manner, optionally with pharmaceutically acceptable carriers. Suitable methods of administering such modulators are available and well known to those of skill in the art, and, although more than one route can be used to administer a particular composition, a particular route can often provide a more immediate and more effective reaction than another route.

Pharmaceutically acceptable carriers are determined in part by the particular composition being administered, as well as by the particular method used to administer the composition. Accordingly, there is a wide variety of suitable formulations of pharmaceutical compositions of the present invention (*see, e.g., Remington's Pharmaceutical Sciences*, 17th ed. 1985)).

The taste modulators, alone or in combination with other suitable components, can be made into aerosol formulations (*i.e.*, they can be “nebulized”) to be administered via inhalation. Aerosol formulations can be placed into pressurized acceptable propellants, such as dichlorodifluoromethane, propane, nitrogen, and the like.

00220-220300

Formulations suitable for administration include aqueous and non-aqueous solutions, isotonic sterile solutions, which can contain antioxidants, buffers, bacteriostats, and solutes that render the formulation isotonic, and aqueous and non-aqueous sterile suspensions that can include suspending agents, solubilizers, thickening agents, stabilizers, and preservatives. In the practice of this invention, compositions can be administered, for example, by orally, topically, intravenously, intraperitoneally, intravesically or intrathecally. Optionally, the compositions are administered orally or nasally. The formulations of compounds can be presented in unit-dose or multi-dose sealed containers, such as ampules and vials. Solutions and suspensions can be prepared from sterile powders, granules, and tablets of the kind previously described. The modulators can also be administered as part a of prepared food or drug.

The dose administered to a patient, in the context of the present invention should be sufficient to effect a beneficial response in the subject over time. The dose will be determined by the efficacy of the particular taste modulators employed and the condition of the subject, as well as the body weight or surface area of the area to be treated. The size of the dose also will be determined by the existence, nature, and extent of any adverse side-effects that accompany the administration of a particular compound or vector in a particular subject.

In determining the effective amount of the modulator to be administered in a physician may evaluate circulating plasma levels of the modulator, modulator toxicities,, and the production of anti-modulator antibodies. In general, the dose equivalent of a modulator is from about 1 ng/kg to 10 mg/kg for a typical subject.

For administration, taste modulators of the present invention can be administered at a rate determined by the LD-50 of the modulator, and the side-effects of the inhibitor at various concentrations, as applied to the mass and overall health of the subject. Administration can be accomplished via single or divided doses.

VIII. Kits

T2R genes and their homologs are useful tools for identifying taste receptor cells, for forensics and paternity determinations, and for examining taste transduction. T2R family member-specific reagents that specifically hybridize to T2R nucleic acids, such as T2R probes and primers, and T2R specific reagents that specifically bind to a T2R protein, *e.g.*, T2R antibodies are used to examine taste cell expression and taste transduction regulation.

Nucleic acid assays for the presence of DNA and RNA for a T2R family member in a sample include numerous techniques are known to those skilled in the art, such as Southern analysis, northern analysis, dot blots, RNase protection, S1 analysis, amplification techniques such as PCR and LCR, and *in situ* hybridization. In *in situ* hybridization, for example, the target nucleic acid is liberated from its cellular surroundings in such as to be available for hybridization within the cell while preserving the cellular morphology for subsequent interpretation and analysis. The following articles provide an overview of the art of *in situ* hybridization: Singer *et al.*, *Biotechniques* 4:230-250 (1986); Haase *et al.*, *Methods in Virology*, vol. VII, pp. 189-226 (1984); and *Nucleic Acid Hybridization: A Practical Approach* (Hames *et al.*, eds. 1987). In addition, a T2R protein can be detected with the various immunoassay techniques described above. The test sample is typically compared to both a positive control (*e.g.*, a sample expressing a recombinant T2R protein) and a negative control.

The present invention also provides for kits for screening for modulators of T2R family members. Such kits can be prepared from readily available materials and reagents. For example, such kits can comprise any one or more of the following materials: T2R nucleic acids or proteins, reaction tubes, and instructions for testing T2R activity. Optionally, the kit contains a biologically active T2R receptor. A wide variety of kits and components can be prepared according to the present invention, depending upon the intended user of the kit and the particular needs of the user.

EXAMPLES

The following examples are provided by way of illustration only and not by way of limitation. Those of skill in the art will readily recognize a variety of noncritical parameters that could be changed or modified to yield essentially similar results.

Example I--Identification of the T2R gene family

Recent genetic linkage studies in humans identified a locus at 5p15 that is associated with the ability to respond to the bitter substance 6-n-propyl-2-thiouracil (PROP; Reed *et al.*, *Am. J. Hum. Genet.* 64:1478-1480 (1999)). To determine whether differences in PROP sensitivity reflected functional differences in a bitter taste receptor, DNA sequence databases were searched for genes encoding candidate transmembrane proteins at this location. Analysis of open reading frames in 450 kb of DNA spanning six

sequenced human genomic BAC clones(see, e.g., accession number AC003015) from this interval identified a novel GPCR (T2R1) at 5p15.2. T2R1 has seven putative transmembrane segments as well as several conserved residues often present in GPCRs (Probst *et al.*, *DNA Cell. Biol.* 11:1-20 (1992)).

5 Computer searches using T2R1, and reiterated with T2R1-related sequences, revealed 19 additional human receptors (12 full-length and 7 pseudogenes). Full-length hT2Rs were isolated by PCR amplification of genomic DNA. Full-length hT2Rs were used to probe a rat circumvallate cDNA library (Hoon *et al.*, *Cell*, 96:541-551 (1999)) and mouse BAC filter arrays (Genome Systems) at low stringency (50-55 °C wash in 1 X SSC). Southern hybridization experiments were used to identify a non-redundant set of positive BACs and to order overlapping BACs.

 These new receptors, referred to as T2Rs (also known as “SF”), define a novel family of GPCRs that are distantly related to V1R vomeronasal receptors and opsins. In contrast to T1Rs, which belong to the superfamily of GPCRs characterized by a large N-terminal domain (Hoon *et al.*, *Cell*, 96:541-551 (1999)), the T2Rs have only a short extracellular N-terminus. Individual members of the T2R-family exhibit 30-70% amino acid identity, and most share highly conserved sequence motifs in the first three and last transmembrane segments, and also in the second cytoplasmic loop. The most divergent regions between T2Rs are the extracellular segments, extending partway into the transmembrane helices. Presumably, the high degree of variability between T2Rs reflects the need to recognize many structurally diverse ligands. Like many other GPCR genes, T2Rs do not contain introns that interrupt coding regions.

Example II--Organization of human T2R genes.

25 The identified human T2R genes are localized on three chromosomes, and are often organized as head-to-tail arrays. For example, four receptor genes are clustered within a single PAC clone from 7q31 and nine in a BAC clone from 12p13. There may be more human T2Rs in these arrays, as several additional human T2Rs were found within partially sequenced BAC clones that overlap the 9 gene T2R cluster. Within a given array, the similarity of receptors is highly variable, including both relatively related (e.g. hT2R13, hT2R14 and hT2R15), and highly divergent receptors (e.g. hT2R3 and hT2R4). This type of organization is mirrored in the mouse (see below), and resembles the genomic organization that has been observed for olfactory receptor genes in humans, mice, flies and worms (Rouquier *et al.*, *Nat. Genet.* 18:243-250 (1998)); Sullivan *et al.*,

PNAS 93:884-888 (1996)); Clyne *et al.*, *Neuron* 22:327-388 (1999)); Voss hall *et al.*, *Cell* 96:725-736 (1999)); Troemel *et al.*, *Cell* 83:207-218 (1995)).

To obtain estimates of the size of this gene family, various genomic resources were examined. Analysis of the Genome Sequence Survey database (gss) yielded 12 partial T2R sequences. Because this database represents an essentially random sampling of ~14% of the human genome, this number suggests that there may be ~90 T2R genes in the human genome. Similar searches of the finished (nr) and unfinished high-throughput human genomic sequence databases (htgs) produced 36 full-length and 15 partial T2R sequences. These databases contain ~50% of the genome sequence, also pointing to ~100 T2R genes in the genome. Recognizing that this analysis may be inaccurate due to the quality of the available databases, and the clustered, non-random distribution of T2Rs in the human genome, it is estimated that the T2R family consists of between 80 to 120 members. However, more than 1/3 of the full-length human T2Rs are pseudogenes; thus, the final number of functional human receptors may be significantly smaller (*i.e.*, 40-80). This is similar to what has been observed for human olfactory receptors, where many of the genes appear to be pseudogenes (Rouquier *et al.*, *Nat. Genet.* 18:243-250 (1998)).

Example III--T2R genes are linked to loci involved in bitter taste

The genetics of sweet and bitter tasting has been extensively studied in mice, where a number of loci influencing responses to sweet and bitter tastants have been mapped by behavioral taste-choice assays (Warren and Lewis, *Nature* 227:77-78 (1970)); Fuller, *J. Hered.* 65:33-66 (1974)). The distal end of mouse chromosome 6 contains a cluster of bitter genes that includes *Soa* (for sucrose octaacetate; Capeless *et al.*, *Behav. Genet.* 22:655-663 (1992)), *Rua* (raffinose undecaacetate; Lush, *Genet. Res.* 47:117-123 (1986)), *Cyx* (cycloheximide; Lush and Holland, *Genet. Res.* 52:207-212 (1988)) and *Qui* (quinine; Lush, *Genet. Res.* 44:151-160 (1984)). Recombination studies indicated that these four loci are closely linked to each other, and to *Prp* (salivary proline rich protein; Azen *et al.*, *Trends Genet.* 2:199-200 (1986)). The human 9 gene T2R cluster contains three interspersed *PRP* genes, and maps to an interval that is homologous with the mouse chromosome 6 bitter cluster.

To define the relationship between the mouse chromosome 6 bitter cluster and T2Rs, a large number of mouse T2R genes were isolated and their genomic organization and physical and genetic map locations were determined. By screening

mouse genomic libraries with human T2Rs, 61 BAC-clones containing 28 mouse T2Rs were isolated. The mouse and human receptors display significant amino acid sequence divergence, but share the sequence motifs common to members of this novel family of receptors. Mouse T2Rs were mapped using a mouse/hamster radiation hybrid panel
5 (Research Genetics), and by examining the strain distribution pattern of single nucleotide polymorphisms in a panel of C57BL/6J x DBA/2J recombinant inbred lines (Jackson Laboratory). These studies showed that the mouse genes are clustered at only a few genomic locations. Each genomic interval containing mouse T2Rs is homologous to one containing its closest human counterpart: mT2R8 and hT2R4, mT2R18 and hT2R16, and
10 mT2R19 and hT2R1. Of these 3 sets of potentially orthologous pairs of human/mouse receptors, both the human T2R1 and T2R16 genes map to locations implicated in human bitter perception (Conneally *et al.*, *Hum. Hered.* 26:267-271 (1976); Reed *et al.*, *Am. J. Hum. Genet.* 64:1478-1480 (1999)). The remaining 25 mT2Rs all map to the distal end of chromosome 6, and are represented by 3 BAC contigs spanning at least 400 kb.

15 Since *Prp* and the bitter-cluster also map to the distal end of mouse chromosome 6, it was determined whether they *localize* within this array of T2Rs. Analysis of a DBA/2 x C57BL/6 recombinant inbred panel revealed that receptors within all 3 BAC-contigs co-segregate with *Prp* and the bitter cluster. Further, the mouse *Prp* gene was isolated (accession number M23236, containing *D6Mit13*) and shown that it lies
20 within the large chromosome 6 T2R cluster. These results demonstrate that T2Rs are intimately linked to loci implicated in bitter perception.

Example IV--T2Rs are expressed in taste receptor cells

The lingual epithelium contains taste buds in three types of papillae:
25 circumvallate papillae at the very back of the tongue, foliate papillae at the posterior lateral edge of the tongue, and fungiform papillae *dispersed* throughout the front half of the tongue surface. Other parts of the oral cavity also have taste buds; these are particularly prominent in the palate epithelium in an area known as the geschmackstreifen and in the epiglottis. To examine the patterns of expression of T2Rs, *in situ*
30 hybridizations were performed using sections of various taste papillae. To ensure that the probes used were expressed in taste tissue, a rat circumvallate cDNA library was screened, leading to the isolation of 14 rat T2Rs cDNAs, each of which is an ortholog of a mouse genomic clone.

To carry out the *in situ* hybridization, tissue was obtained from adult rats and mice. No sex-specific differences of expression patterns were observed, therefore male and female animals were used interchangeably. Fresh frozen sections (16 μ m) were attached to silanized slides and prepared for *in situ* hybridization as described previously (Hoon *et al.*, *Cell*, 96:541-551 (1999)). All *in situ* hybridizations were carried out at high stringency (hybridization, 5 X SSC, 50% formamide, 65-72°C; washing, 0.2 X SSC, 72°C). Signals were developed using alkaline-phosphatase conjugated antibodies to digoxigenin and standard chromogenic substrates (Boehringer Mannheim). Where possible, probes contained extensive 3'-non translated sequence to minimize potential cross-hybridization between T2Rs, which was not observed at the stringency used for *in situ* hybridization.

These experiments demonstrated that T2Rs are selectively expressed in subsets of taste receptor cells of the tongue and palate epithelium. Each receptor hybridizes to an average of 2 cells per taste bud per section. Since the sections used in these experiments contain 1/5-1/3 the depth of a taste bud, this reflects a total of 6-10 positive cells/taste bud/probe (or about 15% of the cells in a taste bud). Examination of serial sections demonstrated that all of the taste buds of the circumvallate papilla contain cells that are positive for each of these probes. Thus far, comparable results have been observed with 11 rat T2Rs, and in mouse sections hybridized with 17 different mT2R probes.

Similar studies in foliate, geschmackstreifen and epiglottis taste buds demonstrated that each receptor probe also labels approximately 15% of the cells in every taste bud. In contrast, T2Rs are rarely expressed in fungiform papillae. Examination of hundreds of fungiform taste buds using 11 different T2R probes demonstrated that less than 10% of all fungiform papillae contain T2R-expressing cells. Interestingly, the few fungiform taste buds that do express T2Rs regularly contain multiple positive cells. In fact, the number of positive cells in these papillae is not significantly different from that seen in taste buds from other regions of the oral cavity. Furthermore, fungiform papillae that contain T2R-expressing cells generally appear clustered. This unexpected finding may provide an important clue about the logic of taste coding. It is known that single fibers of the chorda tympani nerve innervate multiple cells in a fungiform taste bud, and that the same fiber often projects to neighboring papillae (Miller, *J. Comp. Neurol.* 158:155-166 (1974)). Perhaps the non-random distribution of T2R-positive taste receptor

cells and taste buds in fungiform papillae reflect a map of connectivity between similar cells.

Northern analysis and *in situ* hybridization demonstrated that T2Rs are not widely expressed outside taste tissue.

5

Example V--Individual receptor cells express multiple T2R receptors

The above-described results demonstrated that any given T2R is expressed in ~15% of the cells of circumvallate, foliate and palate taste buds. Given that there are over 30 T2Rs in the rodent genome, a taste cell must express more than one receptor. To determine how many receptors are expressed in any cell, and what fraction of taste receptor cells express T2Rs, the number of circumvallate cells labeled with various mixes of 2, 5 or 10 receptors was compared with those labeled with the corresponding individual probes. By counting positive cells in multiple serial sections, it was determined that the number of taste cells labeled with the mixed probes (~20%) was only slightly larger than that labeled by any individual receptor (~15%). Not surprisingly, the signal intensity was significantly enhanced in the mixed probe hybridizations. Similar results were observed in taste buds from other regions of the oral cavity including the fungiform papillae. To directly demonstrate co-expression, double labeling experiments were carried out using a collection of differentially labeled cRNA probes. For double-label fluorescent detection, probes were labeled either with fluorescein or with digoxigenin. An alkaline-phosphatase conjugated anti-fluorescein antibody (Amersham) and a horseradish-peroxidase conjugated anti-digoxigenin antibody were used in combination with fast-red and tyramide fluorogenic substrates (Boehringer Mannheim and New England Nuclear). In these experiments, the majority of cells were found to express multiple receptors.

Example VI--T2R genes are selectively expressed in gustducin-expressing cells

Previous results had shown that T1Rs are expressed in ~30% of taste receptor cells. *In situ* hybridizations with differentially labeled T1R and T2R probes showed that there is no overlap in the expression of these two classes of receptors. Gustducin is also expressed in a large subset of taste receptor cells, but for the most part is not co-expressed with T1Rs (Hoon *et al.*, *Cell*, 96:541-551 (1999)). To determine if T2Rs are expressed in gustducin cells, *in situ* hybridizations were performed using differentially labeled T2Rs and gustducin riboprobes. These experiments demonstrated

that T2Rs are exclusively expressed in gustducin-positive cells of the tongue and palate taste buds.

Approximately 1/3 of the gustducin cells in the circumvallate, foliate and palate taste buds did not label with a mix of 10 T2R probes, suggesting that not all gustducin-expressing cells express T2Rs. These cells may express other, perhaps more distantly related receptors, or could be at a different developmental stage. In fungiform taste buds the situation is quite different. Since only 10% of fungiform taste buds contain T2R positive cells, the great majority of gustducin-positive cells in the front of the tongue do not appear to co-express members of the T2R family of receptors. Therefore, there is likely to be an additional set of receptors expressed in the gustducin-positive cells of fungiform papillae.

Example VII--Functional expression of T2Rs

T2Rs were expressed in conjunction with G α 15, a G-protein α -subunit that has been shown to couple a wide range of receptors to phospholipase C β (Offermanns and Simon, *J Biol Chem*, 270:15175-80 (1995); Krautwurst *et al.*, *Cell* 95:917-926 (1998)). In this system, receptor activation leads to increases in intracellular calcium [Ca $^{2+}$]_i, which can be monitored at the single cell level using the FURA-2 calcium-indicator dye (Tsien *et al.*, *Cell Calcium* 6:145-157 (1985)). To test and optimize G α 15 coupling, two different GPCRs, a G α i-coupled μ -opioid receptor (Reisine, *Neuropharm.* 34:463-472 (1995)) and a G α q-coupled mGluR1 receptor (Masu *et al.*, *Nature* 349:760-765 (1991)), were used. Transfection of these receptors into HEK-293 cell produced robust, agonist-selective, and G α 15-dependent Ca $^{2+}$ responses (Figure 1).

A number of studies have shown that many GPCRs, in particular sensory receptors, require specific "chaperones" for maturation and targeting through the secretory pathway (Baker *et al.*, *Embo J* 13:4886-4895 (1994); Dwyer *et al.*, *Cell* 93:455-466 (1998)). Recently, Krautwurst *et al.* (*Cell* 95:917-926 (1998)) generated chimeric receptors consisting of the first 20 amino acids of rhodopsin and various rodent olfactory receptors. These were targeted to the plasma membrane and functioned as odorant receptors in HEK-293 cells. To determine whether rhodopsin sequences can also help target T2Rs to the plasma membrane, rhodopsin-T2R chimeras (rho-T2Rs) were constructed. Expression of these fusion proteins demonstrated that the first 39 amino

acids of bovine rhodopsin are very effective in targeting T2Rs to the plasma membrane of HEK-293 cells (Figure 2). Similar results were obtained with 11 human and 16 rodent T2Rs (see below). To further enhance the level of T2R expression, rho-T2Rs were placed under the control of a strong EF-1 α promoter, and introduced as episomal plasmids into modified HEK-293 cells expressing G α 15 (pEAKrapid cells).

A bridge overlap PCR extension technique was used to generate rho-T2R chimeras, which contain the first 39 amino acids of bovine rhodopsin in frame with human and rodent T2R coding sequences (Mehta and Singh, *Biotechniques* 26:1082-1086 (1999). All receptors were cloned into a pEAK10 mammalian expression vector (Edge Biosystems, MD). Modified HEK-293 cells (PEAK^{rapid} cells; Edge BioSystems, MD) were grown and maintained at 37 °C in UltraCulture medium (Bio Whittaker) supplemented with 5% fetal bovine serum, 100 μ g/ml Gentamycin sulphate (Fisher), 1 μ g/ml Amphotericin B and 2 mM GlutaMax I (Lifetechnologies). For transfection, cells were seeded onto matrigel coated 24-well culture plates or 35 mm recording chambers. After 24 h at 37 °C, cells were washed in OptiMEM medium (Lifetechnologies) and transfected using LipofectAMINE reagent (Lifetechnologies). Transfection efficiencies were estimated by co-transfection of a GFP reporter plasmid, and were typically >70%. Immunofluorescence staining, and activity assays were performed 36-48 h after transfection.

For immunostaining, transfected cells were grown on coated glass coverslips, fixed for 20 min in ice-cold 2% paraformaldehyde, blocked with 1% BSA, and incubated for 4-6 h at 4 °C in blocking buffer containing a 1:1000 dilution of anti-rhodopsin mAb B6-30 (Hargrave, *et al. Exp Eye Res* 42:363-373 (1986)). Chimeric receptor expression was visualized using FITC-coupled donkey anti-mouse secondary antibodies (Jackson Immunochemical).

Two parallel strategies were employed to identify ligands for T2Rs. In one, a random set of human, rat and mouse T2R receptors were selected and individually tested against a collection of 55 bitter and sweet tastants, including (shown with maximum concentrations tested): 5 mM aristolochic acid, 5 mM atropine, 5 mM brucine, 5 mM caffeic acid, 10 mM caffeine, 1 mM chloroquine, 5 mM cycloheximide, 10 mM denatonium benzoate, 5 mM (-) epicatechin, 10 mM L-leucine, 10 mM L-lysine, 10 mM MgCl₂, 5 mM naringin, 10 mM nicotine, 2.5 mM papavarine hydrochloride, 3 mM phenyl thiocarbamide, 10 mM 6-n-propyl thiouracil, 1 mM quinacrine, 1 mM quinine

hydrochloride, 800 μ M raffinose undecaacetate, 3 mM salicin, 5 mM sparteine, 5 mM strychnine nitrate, 3 mM sucrose octaacetate, 2 mM tetraethyl ammonium chloride, 10 mM L-tyrosine, 5 mM yohimbine, 10 mM each of L-glycine, L-alanine, D-tryptophan, L-phenylalanine, L-arginine, sodium saccharin, aspartame, sodium cyclamate, acesulfame K, 150 mM each of sucrose, lactose, maltose, D-glucose, D-fructose, D-galactose, D-sorbitol, 0.1% monellin, 0.1% thaumatin. Additional sweet tastants were 150 μ M alitame, 1.8 mM dulcin, 800 μ M stevioside, 1.9 mM cyanosusan, 600 μ M neohesperidin dihydrochalcone, 10 mM xylitol, 9.7 mM H-Asp-D-Ala-OTMCP, 70 μ M N-Dmb-L-Asp-L-Phe-Ome, and 12 μ M N-Dmb-L-Asp-D-Val-(S)- α methylbenzylamide. In these assays, functional coupling was assessed based on four criteria: tastant selectivity, temporal specificity, and receptor- and G protein-dependence. The second strategy relied upon data on the genetics of bitter perception in mice to link candidate receptors with specific tastants.

Nearly 30 years ago, it was first reported that various inbred strains of mice differ in their sensitivity to the bitter compound sucrose-octaacetate (Warren and Lewis, *Nature* 227:77-78 (1970)). Subsequently, a number of studies demonstrated that this strain difference was due to allelic variation at a single genetic locus (Soa) (Whitney and Harder, *Behav Genet* 16:559-574 (1986); Capeless *et al.*, *Behav Genet* 22:655-663 (1992)). These findings were extended to additional loci influencing sensitivity to various bitter tastants, including raffinose undecaacetate (Rua), cycloheximide (Cyx), copper glycinate (Glb), and quinine (Qui) (Lush, *Genet. Res.* 44:151-160 (1984); Lush, *Genet. Res.* 47:117-123 (1986), Lush and Holland, (1988)). Genetic mapping experiments showed that the Soa, Rua, Cyx, Qui and Glb loci are clustered at the distal end of chromosome 6 (Lush and Holland, *Genet. Res.* 52:207-212 (1988); Capeless *et al.*, *Behav Genet* 22:655-663 (1992)). In view of the above-described localization of various T2R genes to bitter-associated loci in mice, T2R receptors from this array were constructed as corresponding rho-mT2R chimeras and individually transfected into HEK-293 cells expressing the promiscuous G α 15 protein. After loading the cells with FURA-2, responses to sucrose octaacetate, raffinose undecaacetate, copper glycinate, quinine, and cycloheximide were assayed.

Transfected cells were washed once in Hank's balanced salt solution with 1 mM sodium pyruvate and 10 mM HEPES, pH 7.4 (assay buffer), and loaded with 2 μ M FURA-2 AM (Molecular Probes) for 1 h at room temperature. The loading solution was

removed and cells were incubated in 200 μ l of assay buffer for 1 h to allow the cleavage of the AM ester. For most experiments, 24-well tissue culture plates containing cells expressing a single rho-T2R were stimulated with 200 μ l of a 2x tastant solution (see next section). $[Ca^{2+}]_i$ changes were monitored using a Nikon Diaphot 200 microscope equipped with a 10x/0.5 fluor objective with the TILL imaging system (T.I.L.L Photonics GmbH). Acquisition and analysis of the fluorescence images used TILL-Vision software. Generally, $[Ca^{2+}]_i$ was measured for 80 - 120 s by sequentially illuminating cells for 200ms at 340nm and 380nm and monitoring the fluorescence emission at 510nm using a cooled CCD camera. The F_{340}/F_{380} ratio was analyzed to measure $[Ca^{2+}]_i$.

Kinetics of activation and deactivation were measured using a bath perfusion system. Cells were seeded onto a 150 μ l microperfusion chamber, and test solutions were pressure-ejected with a picospritzer apparatus (General Valve, Inc.). Flow-rate was adjusted to ensure complete exchange of the bath solution within 4-5 s. In the case of mT2R5, the entire camera field was measured since >70% of the cells responded to cycloheximide. For mT2R8 and hT2R4, 100 areas of interest in each were averaged for each experiment.

Cells expressing mT2R5 specifically responded to cycloheximide (Figure 3). The response occurred in nearly all transfected cells and was receptor- and $G\alpha_{15}$ -dependent because cells lacking either of these components did not trigger $[Ca^{2+}]_i$ changes, even at 5000-fold higher cycloheximide concentration. As expected for this coupling system, the tastant-induced increase in $[Ca^{2+}]_i$ was due to release from internal stores, since analogous results were obtained in nominally zero $[Ca^{2+}]_{out}$. The activation of mT2R5 by cycloheximide is very selective, as this receptor did not respond to any other tastants, even at concentrations that far exceeded their biologically relevant range of action (Saroli, *Naturwissenschaften* 71:428-9 (1984); Glendinning, *Behav Neurosci* 113:840-854 (1994))(Figure 4a,b). While cycloheximide is only moderately bitter to humans, it is strongly aversive to rodents with a sensitivity threshold of ~ 0.25 μ M (Kusano *et al.*, *Appl. Exptl. Zool.* 6:40-50 (1971); Lush and Holland, *Genet. Res.* 52:207-212 (1988)). In the cell-based assay described herein, the concentration of cycloheximide required to induce half-maximal response of mT2R5 was 0.5 μ M, and the threshold was ~ 0.2 μ M (Figure 4c,d). Notably, this dose-response closely matches the sensitivity range of cycloheximide tasting in mice.

To examine the kinetics of the cycloheximide response, rho-mT2R5 transfected cells were placed on a microperfusion chamber and superfused with test solutions under various conditions. The cells showed robust transient responses to micromolar concentrations of cycloheximide that closely follow application of the stimulus (latency <1 s). As expected, when the tastant was removed, [Ca²⁺]_i returned to baseline. A prolonged exposure to cycloheximide (>10 s) resulted in adaptation: a fast increase of [Ca²⁺]_i followed by a gradual, but incomplete decline to the resting level (Figure 4a). Similarly, successive applications of cycloheximide led to significantly reduced responses, indicative of desensitization (Lefkowitz *et al.*, *Cold Spring Harb Symp Quant Biol* 57:127-133 (1992)). This is likely to occur at the level of the receptor, since responses of a control, co-transfected mGluR1 were not altered during the period of cycloheximide desensitization.

To determine whether other T2Rs are also activated by bitter compounds, rhodopsin-tagged human T2R receptors were assayed by individually transfecting them into HEK-293 cells expressing Gα15. Each transfected line was tested against a battery of bitter and sweet tastants, including amino acids, peptides, and other natural and synthetic compounds. These experiments demonstrated that the intensely bitter tastant denatonium induced a significant transient increase in [Ca²⁺]_i in cells transfected with one of the human candidate taste receptors, hT2R4, but not in control untransfected cells (Figure 3), or in cells transfected with other hT2Rs. The denatonium response had a strong dose-dependency with a threshold of ~100 μM. Interestingly, hT2R4 displayed a limited range of promiscuity since it also responded to high concentrations of the bitter tastant 6-n-propyl-2-thiouracil (PROP) (Figure 5).

If the responses of hT2R4 reflect the *in vivo* function of this receptor, it was hypothesized that similarly tuned receptors might be found in other species. The mouse receptor mT2R8 is a likely ortholog of hT2R4: they share ~ 70% identity, while the next closest receptor is only 40% identical; these two genes are contained in homologous genomic intervals. A rho-mT2R8 chimeric receptor was generated and examined for its response to a wide range of tastants. Indeed, mT2R8, like its human counterpart, is activated by denatonium and by high concentrations of PROP (Figures 3 and 5). No other tastants elicited significant responses from cells expressing mT2R8. Because these two receptors share only 70% identity, the similarity in their responses to bitter compounds attests to their role as orthologous bitter taste receptors.

Example VIII--Cycloheximide non-taster mice have mutations in the mT2R5 taste receptor

The demonstration that mT2R5 functions as a high affinity receptor for cycloheximide suggested that the mT2R5 gene might correspond to the Cyx locus. *In situ* hybridization to tissue sections demonstrated that the expression profile of mT2R5 is indistinguishable between taster and non-taster strains (Figure 6). To determine the linkage between mT2R5 and the Cyx locus, polymorphisms in the mT2R5 gene were identified and their distribution in a recombinant inbred panel from a C57BL/6J (non-taster) x DBA/2J (taster) cross was determined. Tight linkage was found between mT2R5 and the Cyx locus. To test the possibility that mutations in the mT2R5 gene were responsible for the Cyx phenotype, the mT2R5 gene was isolated from several additional well-characterized cycloheximide taster (CBA/Ca, BALB/c, C3H/He) and non-taster (129/Sv) strains and their nucleotide sequences determined. Indeed, as would be expected if mT2R5 functions as the cycloheximide receptor in these strains, all the tasters share the same mT2R5 allele as DBA/2J, while the non-tasters share the C57BL/6 allele, which carries missense mutations (Figure 6), including 3 non-conservative amino acid substitutions (T44I, G155D and L294R).

If the mT2R5 C57BL/6 allele is responsible for the taste deficiency of Cyx mutants, its cycloheximide dose-response might recapitulate the sensitivity shift seen in Cyx mutant strains. Two-bottle preference tests have shown that Cyx taster strains avoid cycloheximide with a threshold of 0.25 μ M, while non-tasters have a \sim 8-fold decrease in sensitivity (*e.g.* they, are non-tasters at 1 μ M, but strongly avoid cycloheximide at 8 μ M). A rho-mT2R5 fusion was constructed with the mT2R5 gene from a non-taster strain, and its dose response compared with that of the receptor from taster strains. Remarkably, mT2R5 from the non-taster strains displays a shift in cycloheximide sensitivity (Figure 4d) that resembles the sensitivity of these strains to this bitter tastant. Taken together, these results validate mT2R5 as a cycloheximide receptor, and strongly suggest that mT2R5 corresponds to the Cyx locus.

Example IX--T2Rs couple to gustducin

The above-described demonstration that T2Rs are co-expressed with gustducin suggests that T2Rs activate this G-protein in response to bitter tastants. To

investigate the selectivity of T2R - G-protein coupling, mT2R5 was chosen for study because its activation by cycloheximide recapitulates mouse taste responses. Rho-tagged mT2R5 and gustducin were prepared using a baculovirus expression system. mT2R5-containing membranes were incubated with various purified G-proteins, including

5 gustducin, and measured tastant-induced GTP- γ S binding (Hoon *et al.*, *Biochem J* 309:629-636 (1995)). Specifically, infectious Bacmid containing rhodopsin tagged mT2R5 (DBA/2-allele) was produced using the Bac-to-Bac system (Lifetechnologies, MD). Insect larval cells were infected for 60 h with recombinant Bacmid and membranes were prepared as described previously (Ryba and Tirindelli, *J Biol Chem*, 270:6757-6767

10 (1995)). Peripheral proteins were removed by treatment with 8 M urea and membranes were resuspended in 10 mM HEPES pH7.5, 1 mM EDTA and 1 mM DTT. The expression of rho-mT2R5 was assessed by Western blot using mAb B6-30 and quantitated by comparison with known amounts of rhodopsin. Approximately 300 pmol of rho-mT2R5 could be obtained from 2×10^8 infected cells. Gustducin and G $\beta_1\gamma_8$

15 heterodimers were isolated as described previously (Hoon *et al.*, *Biochem J* 309:629-636 (1995); Ryba and Tirindelli, *J Biol Chem*, 270:6757-6767 (1995)). Receptor-catalyzed exchange of GDP for GTP γ S on gustducin and other G-protein α -subunits was measured in the presence of 10 nM rho-mT2R5, 100 μ M GDP, and 20 μ M G $\beta_1\gamma_8$. All measurements were made at 15-minute time points, and reflect the initial rate of GTP γ S

20 binding.

These GTP- γ S binding assays revealed exquisite cycloheximide-dependent coupling of mT2R5 to gustducin (Figure 7). In contrast, no coupling was seen with G α_s , G α_i , G α_q or G α_o . No significant GTP γ S binding was observed in the absence of receptor, gustducin or $\beta\gamma$ -heterodimers. The high selectivity of T2R5 for gustducin, and

25 the exclusive expression of T2Rs in taste receptor cells that contain gustducin, affirm the hypothesis that T2Rs function as gustducin-linked taste receptors.

All publications and patent applications cited in this specification are

30 herein incorporated by reference as if each individual publication or patent application were specifically and individually indicated to be incorporated by reference.

Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be readily

SEQUENCE LISTING

SEQ ID NO:1

Human T2R01 amino acid sequence

5

MLESHLIIYFLLAVIQFLLGIFTNGIIVVNGIDLIKHRKMAPLDLLLSCLAVSRI FLQL
FIFYVNVIVIFFIEFIMCSANCAILLFINELELWLATWLGVFYCAKVASVRHPLFIWLKM
RISKLVPMILGSLLYVSMICVFHFSKYAGFMVPYFLRKFFSQNATIQKEDTLAIQIFSFV
AEFSVPLLI FLFAVLLLI FSLGRHTRQMRNTVAGSRVPGRGAPISALLSILSFLILYFSH
10 CMIKVFLSSLKFHIRRFIFLFFILVIGIYPSGHSLLILILGNPKLKQNAKKFLLHSKCCQ

SEQ ID NO:2

Human T2R01 nucleotide sequence

15

ATGCTAGAGTCTCACCTCATTATCTATTTTCTTCTTGCAGTGATACAATTTCTTCTTGGG
ATTTTCACAAATGGCATCATTGTGGTGGTGAATGGCATTGACTTGATCAAGCACAGAAAA
ATGGCTCCGCTGGATCTCCTTCTTTCTTGTCTGGCAGTTTCTAGAATTTTCTGCAGTTG
TTCATCTTCTACGTTAATGTGATTGTTATCTTCTTCATAGAATTCATCATGTGTTCTGCG
20 AATTGTGCAATTCTCTTATTTATAAATGAATTGGAACTTTGGCTTGCCACATGGCTCGGC
GTTTTCTATTGTGCCAAGGTTGCCAGCGTCCGTCACCCACTCTTCATCTGGTTGAAGATG
AGGATATCCAAGCTGGTCCCATGGATGATCCTGGGGTCTCTGCTATATGTATCTATGATT
TGTGTTTTCCATAGCAAATATGCAGGGTTTATGGTCCCATACTTCCTAAGGAAATTTTTC
TCCCAAATGCCACAATTCAAAAAGAAGATACACTGGCTATACAGATTTTCTCTTTTGT
25 GCTGAGTTCTCAGTGCCATTGCTTATCTTCCTTTTGTCTGTTTTGCTCTTGATTTTCTCT
CTGGGGAGGCACACCCGGCAAATGAGAAACACAGTGGCCGGCAGCAGGGTTCTGGCAGG
GGTGCACCCATCAGCGCGTTGCTGTCTATCCTGTCCTTCCTGATCCTCTACTTCTCCAC
TGCATGATAAAAGTTTTTCTCTCTTCTCTAAAGTTTCACATCAGAAGGTTTCATCTTTCTG
TTCTTCATCCTTGTGATTGGTATATACCCTTCTGGACACTCTCTCATCTTAATTTTAGGA
30 AATCCTAAATTGAAACAAAATGCAAAAAGTTTCCTCCTCCA**CAGTAAGTGCTGTCAGTGA**

SEQ ID NO:3

Human T2R02 amino acid sequence

MALSFSAILHIIMMSAEFFTGITVNGFLIIVNCNELIKHRKLMPIQILLMCIGMSRFGLO
MVL MVQSFFSVFFPLLYVKIIYGAAMMFLWMFFSSISLWFATCLSVFYCLKISGFTQSCF
LWLKFRIPKLIPWLFWEAFWPL*ALHLCVEVDYAKNVEEDALRNTTLKKSCTKIKKISEV
5 LLVNLALIFPLAIFVMCTSMLLISLYKHTHRMQHSGHGFERNANTEAHINALKTVITFFCF
FISYFAAFMTNMTFSLPYRSHQFFMLKDIMAAYPSGHSVIIILSNSKFQQSFRILCLKK
KL

10 **SEQ ID NO:4**

Human T2R02 nucleotide sequence

ATGGCCTTGTCTTTTTCAGCTATTCTTCATATTATCATGATGTCAGCAGAATTCTTCACA
GGGATCACAGTAAATGGATTTCTTATCATTGTAACTGTAATGAATTGATCAAACATAGA
15 AAGCTAATGCCAATTCAAATCCTCTTAATGTGCATAGGGATGTCTAGATTTGGTCTGCAG
ATGGTGTTAATGGTACAAAGTTTTTCTCTGTGTTCTTTCCACTCCTTTACGTCAAATA
ATTTATGGTGCAGCAATGATGTTCTTTGGATGTTTTTTAGCTCTATCAGCCTATGGTTT
GCCACTTGCCTTTCTGTATTTTACTGCCTCAAGATTTACGGCTTCACTCAGTCCTGTTTT
CTTTGGTTGAAATTCAGGATCCCAAAGTTAATACCTTGGCTGCTTCTGGGAAGCGTTCTG
20 GCCTCTGTGAGCATTGCATCTGTGTGTGCGAGGTAGATTACGCTAAAAATGTGGAAGAGGA
TGCCCTCAGAAACACCACACTAAAAAAGAGTAAACAAAGATAAAGAAAATTAGTGAAGT
GCTTCTTGTCAACTTGGCATTAAATATTTCTCTAGCCATATTTGTGATGTGCACTTCTAT
GTTACTCATCTCTCTTTACAAGCACACTCATCGGATGCAACATGGATCTCATGGCTTTAG
AAATGCCAACACAGAAGCCCATATAAATGCATTAAAAACAGTGATAACATTCTTTTGCTT
25 CTTTATTTCTTATTTTGCTGCCTTCATGACAAATATGACATTTAGTTTACCTTACAGAAG
TCACCAGTTCTTTATGCTGAAGGACATAATGGCAGCATATCCCTCTGGCCACTCGGTTAT
AATAATCTTGAGTAATTCTAAGTTCCAACAATCATTTAGAAGAATTCTCTG**CCTCAAAAA**
GAAACTATGA

30

SEQ ID NO:5

Human T2R03 amino acid sequence

MMGLTEGVFLILSGTQFTLGILVNCFIELVNGSSWFKTKRMSLSDFIITTLALLRIILLC
IILTDSFLIEFSPNTHDSGIIMQIIDVSWTFTNHL SIWLATCLGVLYCLKIASFSHPTFL
WLKWRVSRVMVWMLLGALLSCGSTASLINEFKLYSVFRGIEATRNVTEHFRKKRSEYYL
IHVLGTLWYLPPLIVSLASYSLLI FSLGRHTRQMLQNGTSSRDP TTEAHKRAIRIILSFF
5 FLFLLYFLAFLIASFGNFLPKTKMAKMIGEVM TMFY PAGHSFILILGNSKLKQTFVVMLR
CESGHLKPGSKGPIFS

SEQ ID NO:6

10 Human T2R03 nucleotide sequence

ATGATGGGACTCACCGAGGGGGTGTTCTGATTCTGTCTGGCACTCAGTTCACACTGGGA
ATTCTGGTCAATTGTTTCATTGAGTTGGTCAATGGTAGCAGCTGGTTCAAGACCAAGAGA
ATGTCTTTGTCTGACTTCATCATCACCACCCTGGCACTCTTGAGGATCATTCTGCTGTGT
15 ATTATCTTGACTGATAGTTTTTTAATAGAATTCTCTCCCAACACACATGATTCAGGGATA
ATAATGCAAATTATTGATGTTTCCTGGACATTTACAAACCATCTGAGCATTGCTTGGC
ACCTGTCTTGGTGTCCTCTACTGCCTGAAAATCGCCAGTTTCTCTACCCCCACATTCCTC
TGGCTCAAGTGGAGAGTTTCTAGGGTGATGGTATGGATGCTGTTGGGTGCACTGCTCTTA
TCCTGTGGTAGTACCGCATCTCTGATCAATGAGTTTAAGCTCTATTCTGTCTTTAGGGGA
20 ATTGAGGCCACCAGGAATGTGACTGAACACTTCAGAAAGAAGAGGAGTGAGTATTATCTG
ATCCATGTTCTTGGGACTCTGTGGTACCTGCCTCCCTTAATTGTGTCCCTGGCCTCCTAC
TCTTTGCTCATCTTCTCCCTGGGGAGGCACACACGGCAGATGCTGCAAATGGGACAAGC
TCCAGAGATCCAACCACTGAGGCCCAAGAGGGGCCATCAGAATCATCCTTTCTTCTTC
TTTCTCTTCTTACTTTACTTTCTTGCTTTCTTAATTGCATCATTTGGTAATTCCTACCA
25 AAAACCAAGATGGCTAAGATGATTGGCGAAGTAATGACAATGTTTTATCCTGCTGGCCAC
TCATTTATTCTCATTCTGGGGAACAGTAAGCTGAAGCAGACATTTGTAGTGATGCTCCGG
TGTGAGTCTGGTCATCTGAAGCCTGGATCCA**AGGGACCCATTTTCTCTTAG**

30 **SEQ ID NO:7**

Human T2R04 amino acid sequence

MLRLFYFSALIASVILNFVGIIMNLFITVVNCKTWVKSHRISSSDRILFSLGITRFLMLG
LFLVNTIYFVSSNTERSVYLSAFFVLCFMFLDSSSVWFVTLNILYCVKITNFQHSVFL

LKRNI SPKIPRLLLACVLISAFTTCLYITLSQASPFPELVTTNRNNTSFNISEGILSLVVS
LVLSSSLQFI INVTSASLLIHSLRRHIQKMQKNATGFWNPQTEAHVGAMKLMVYFLILYI
PYSVATLVQYLPFYAGMDMGTKSICLIFATLYSPGHSVLI I ITHPKLKTTAKKILCFKK

5

SEQ ID NO:8

Human T2R04 nucleotide sequence

ATGCTTCGGTTATTCTATTTCTCTGCTATTATTGCCTCAGTTATTTTAAATTTTGTAGGA
10 ATCATTATGAATCTGTTTATTACAGTGGTCAATTGCAAACTTGGGTCAAAGCCATAGA
ATCTCCTCTTCTGATAGGATTCTGTTCAGCCTGGGCATCACCAGGTTTCTTATGCTGGGA
CTATTTCTGGTGAACACCATCTACTTCGTCTCTTCAAATACGGAAAGGTCAGTCTACCTG
TCTGCTTTTTTTGTGTTGTGTTTCATGTTTTTGGACTCGAGCAGTGTCTGGTTTGTGACC
TTGCTCAATATCTTGTACTGTGTGAAGATTACTAACTTCCAACACTCAGTGTTCCTCCTG
15 CTGAAGCGGAATATCTCCCCAAAGATCCCCAGGCTGCTGCTGGCCTGTGTGCTGATTTCT
GCTTTCACCACTTGCCTGTACATCAGCTTAGCCAGGCATCACCTTTTCCTGAACCTGTG
ACTACGAGAAATAACACATCATTTAATATCAGTGAGGGCATCTTGTCTTTAGTGGTTTCT
TTGGTCTTGAGCTCATCTCTCCAGTTCATCATTAATGTGACTTCTGCTTCCTTGCTAATA
CACTCCTTGAGGAGACATATACAGAAGATGCAGAAAAATGCCACTGGTTTCTGGAATCCC
20 CAGACGGAAGCTCATGTAGGTGCTATGAAGCTGATGGTCTATTTCTCATCCTCTACATT
CCATATTCAGTTGCTACCCTGGTCCAGTATCTCCCCTTTTATGCAGGGATGGATATGGGG
ACCAAATCCATTTGTCTGATTTTGGCCACCCTTTACTCTCCAGGACATTCTGTTCTCATT
ATTATCACACATCCTAAACTGAAAACAACAGCAAA**GAAGATTCTTTGTTTCAAAAAATAG**

25

SEQ ID NO:9

Human T2R05 amino acid sequence

MLSAGLGLLMLVAVVEFLIGLIGNGSLVVWSFREWIRKFNWSSYNLIILGLAGCRFLLQW
30 LIILDLSLFPLFQSSRWLRYLSIFWVLVSQASLWFATFLSVFYCKKITTFDRPAYLWLKQ
RAYNLSLWCLLGIFYFIINLLLTVQIGLTFYHPPQGNSSIRYPFESWQYLYAFQLNSGSYLP
LVVFLVSSGMLIVSLYTHHKMKVHSAGRDRVRAKAHITALKSLGCFLLLHLVYIMASPF
SITSKTYPPDLTSVFIWETLMAAYPSLHSLILIMGIPRVKQTCQKILWKTVCARRCWGP

SEQ ID NO:10

Human T2R05 nucleotide sequence

5 **ATGCTGAGCGCTGGCCTAG**ACTGCTGATGCTGGTGGCAGTGGTTGAATTTCTCATCGGT
TTAATTGGAAATGGAAGCCTGGTGGTCTGGAGTTTTAGAGAATGGATCAGAAAATTCAAC
TGGTCCTCATATAACCTCATTATCCTGGGCCTGGCTGGCTGCCGATTTCTCCTGCAGTGG
CTGATCATTTTTGGACTTAAGCTTGTTCCTTTCCAGAGCAGCCGTTGGCTTCGCTAT
CTTAGTATCTTCTGGGTCCTGGTAAGCCAGGCCAGCTTATGGTTTGCCACCTTCCTCAGT
10 GTCTTCTATTGCAAGAAGATCACGACCTTCGATCGCCCGGCCTACTTGTGGCTGAAGCAG
AGGGCCTATAACCTGAGTCTCTGGTGCCTTCTGGGCTACTTTATAATCAATTGTTACTT
ACAGTCCAAATTGGCTTAACATTCTATCATCCTCCCCAAGGAAACAGCAGCATTCCGGTAT
CCCTTTGAAAGCTGGCAGTACCTGTATGCATTTAGCTCAATTCAGGAAGTTATTTGCCT
TTAGTGGTGTTCCTTGTTCCTCTGGGATGCTGATTGTCTCTTTGTATACACACCACAAG
15 AAGATGAAGGTCCATTAGCTGGTAGGAGGGATGTCCGGGCCAAGGCTCACATCACTGCG
CTGAAGTCCTTGGGCTGCTTCCTCTTACTTCACCTGGTTTATATCATGGCCAGCCCCCTTC
TCCATCACCTCCAAGACTTATCCTCCTGATCTCACCAGTGTCTTCATCTGGGAGACACTC
ATGGCAGCCTATCCTTCTCTTCACTTCTCATATTGATCATGGGGATTCTAGGGTGAAG
CAGACTTGTCAGAAGATCCTGTGGAAGACAGTGTGTGCTCG**GAGATGCTGGGGCCCATGA**
20

SEQ ID NO:11

Human T2R06 amino acid sequence

25 MLAAALGLLMPIAGAEFLIGLVGNVPVVCSEFRGWVKKM*GVPINSHDSGK*PLSPTQAD
HVGHKSVSTFPEQWLALLS*CLRVLVSQANM*FATFFSGFCCMEIMTFVXXXXXXXXXXXX
XXXXXXXXXXLLVSFKITFYFSALVGWTL*KPLTGNSNILHPILNLLFL*IAVQ*RRLIAI
CDVSVPLVFL*RHHRKMEDHTAVRRRLKPRXXXXXXXXXXXXXXXXXLYMVSALARHFSMTF
*SPSDLTILAISATLMAVYTSFPSIVMVMRNQTCQRIL*EMICTWKS
30

SEQ ID NO:12

Human T2R06 nucleotide sequence

ATGTTGGCGGCTGCCCTAGGATTGCTGATGCCCATTCAGGGGCTGAATTTCTCATTGGC
 CTGGTTGGAAATGGAGTCCCTGTGGTCTGCAGTTTTAGAGGATGGGTCAAAAAATGTAA
 GGAGTCCCTATAAATTCTCATGATTCTGGTAAGTAGCCACTTTCTCCTACTCAGGCCGAT
 CATGTTGGACATAAGTCTGTTTCCACTTTCCCAGAGCAGTGGTTGGCTTTACTATCTTAA
 5 TGTCTTCGAGTCCTGGTAAGCCAGGCCAACATGTAGTTTGCCACTTTCTTCAGTGGCTTC
 TGCTGCATGGAGATCATGACCTTTGTCCCGCTGACTTCTTGTAGCTGAAAAGACTGGGTT
 TTTGTTTTTTGCTAGTGTCTTTCAAGATCACTTTTTATTTCTCAGCTCTTGTTGGCTGGA
 CCCTTTAAAAACCCTTAACAGGAAACAGCAACATCCTGCATCCCATTTTAAATCTGTTAT
 TTTTATAGATTGCTGTCCAGTGAAGGAGACTGATTGCTATTTGTGATGTTTCTGTTCCAC
 10 TTGTCTTTTTGTAAAGACATCACAGGAAGATGGAGGACCACACAGCTGTCAGGAGGAGGC
 TCAAACCAAGGTGCTCATCGCTCTGAAGTTCCCCCTTACATGGTTTCTGCCTTGGCCAG
 AACTTTTCCATGACCTTCTAATCTCCCTCTGATCTCACCATTCTTGCCATCTCTGCAAC
 ACTCATGGCTGTTTATACTTCATTTCCGTCTATTGTAATGGTTATGAGGAATCAGACTTG
 TCAGAGAATTCTGTAGGAGATGATATGTACATGGAAATCCTAG

15

SEQ ID NO:13

Human T2R07 amino acid sequence

20 MADKVQTTLLFLAVGEFSVGILGNAFIGLVNCDWVKRKIASIDLILTSLAISRICLLC
 VILLDCFILVLYPDVYATGKEMRIIDFFWTLTNHLSIWFATCLSIYYFFKIGNFFHPLFL
 WMKWRIDRVISWILLGCVVLSVFISLPATENLNADFRFCVKAKRKTNLTWSCRVNKTQHA
 STKLFLNLATLLPFCVCLMSFFLLILSLRRHIRMQLSATGCRDPSTEAHVRALKAVISF
 LLLFIAYYLSFLIATSSYFMPETELAVIFGESIALIYPSSHFILILGNNKLRHASLKVI
 25 WKVMSILKGRKFQQHKQI

SEQ ID NO:14

Human T2R07 nucleotide sequence

30

ATGGCAGATAAAGTGCAGACTACTTTTATTGTTCTTAGCAGTTGGAGAGTTTTCAGTGGGG
 ATCTTAGGGAATGCATTCATTGGATTGGTAAACTGCATGGACTGGGTCAAGAAGAGGAAA
 ATTGCCTCCATTGATTTAATCCTCACAAGTCTGGCCATATCCAGAATTTGTCTATTGTGC
 GTAATACTATTAGATTGTTTTATATTGGTGCTATATCCAGATGTCTATGCCACTGGTAAA

GAAATGAGAATCATTGACTTCTTCTGGACACTAACCAATCATTTAAGTATCTGGTTTGCA
 ACCTGCCTCAGCATTTACTATTTCTTCAAGATAGGTAATTTCTTTCACCCACTTTTCCTC
 TGGATGAAGTGGAGAATTGACAGGGTGATTTCTGATTCTACTGGGGTGCGTGGTTCTC
 TCTGTGTTTATTAGCCTTCCAGCCACTGAGAATTTGAACGCTGATTTCAGGTTTTGTGTG
 5 AAGGCAAAGAGGAAAACAACTTAACTTGGAGTTGCAGAGTAAATAAACTCAACATGCT
 TCTACCAAGTTATTTCTCAACCTGGCAACGCTGCTCCCCCTTTGTGTGTGCCTAATGTCC
 TTTTTCCTCTTGATCCTCTCCCTGCGGAGACATATCAGGCGAATGCAGCTCAGTGCCACA
 GGGTGCAGAGACCCCAGCACAGAAGCCCATGTGAGAGCCCTGAAAGCTGTCATTTCTTC
 CTTCTCCTCTTTATTGCCTACTATTTGTCCTTTCTCATTGCCACCTCCAGCTACTTTATG
 10 CCAGAGACGGAATTAGCTGTGATTTTTGGTGAGTCCATAGCTCTAATCTACCCCTCAAGT
 CATTCATTTATCCTAATACTGGGGAACAATAAATTAAGACATGCATCTCTAAAGGTGATT
 TGGAAAGTAATGTCTATTCTAAAAGGAAGAAAATT**CCAACAACATAAAACAATCTGA**

15 **SEQ ID NO:15**

Human T2R08 amino acid sequence

MFSPADNIFIILITGEFILGILGNGYIALVNWIDWIKKKKISTVDYILTNLVIARICLIS
 VMVNGIVIVLNPDVYTKNKQQIVIFTFWTFANYLNMWITTCLNVFYFLKIASSSHPLFL
 20 WLKWKIDMVVHWILLGCF AISLLVSLIAAIVLSCDYRFHAI AKHKRNITEMFHVSKI PYF
 EPLTLFNLFAIVPFIVSLISFLLVRS LWRHTKQIKLYATGSRDPSTEVHVR AIKMTSF
 IFFFFLYYISSILMTFSYLMTKYKLAVEFGEIAAILYPLGHS LILIVLNNKL RQTFVRML
 TCRKIACMI

25

SEQ ID NO:16

Human T2R08 nucleotide sequence

ATGTT CAGT CCT GCAGATAACATCTTTATAATCCTAATAACTGGAGAATTCATACTAGGA
 30 ATATTGGGGAATGGATACATTGCACTAGTCAACTGGATTGACTGGATTAAAGAAGAAAAAG
 ATTTCCACAGTTGACTACATCCTTACCAATTTAGTTATCGCCAGAATTTGTTTGATCAGT
 GTAATGGTTGTAAATGGCATTGTAATAGTACTGAACCCAGATGTTTATACAAAAAATAAA
 CAACAGATAGTCATTTTTACCTTCTGGACATTTGCCAACTACTTAAATATGTGGATTACC
 ACCTGCCTTAATGTCTTCTATTTTCTGAAGATAGCCAGTTCCTCTCATCCACTTTTTCTC

TGGCTGAAGTGGAAAATTGATATGGTGGTGCACCTGGATCCTGCTGGGATGCTTTGCCATT
 TCCTTGTTGGTCAGCCTTATAGCAGCAATAGTACTGAGTTGTGATTATAGGTTTCATGCA
 ATTGCCAAACATAAAAGAAACATTACTGAAATGTTCCATGTGAGTAAAATACCATACTTT
 GAACCCTTGACTCTCTTTAACCTGTTTGCAATTGTCCCATTTATTGTGTCACTGATATCA
 5 TTTTTCCTTTTAGTAAGATCTTTATGGAGACATACCAAGCAAATAAACTCTATGCTACC
 GGCAGTAGAGACCCCAGCACAGAAGTTCATGTGAGAGCCATTAAAACTATGACTTCATTT
 ATCTTCTTTTTTTTTCCTATACTATATTTCTTCTATTTTGATGACCTTTAGCTATCTTATG
 ACAAATAACAAGTTAGCTGTGGAGTTTGGAGAGATTGCAGCAATTCTCTACCCCTTGGGT
 CACTCACTTATTTTAATTGTTTTAAATAATAAACTGAGGCAGACATTTGTCAGAATGCTG
 10 ACATGTAG**GAAAAATTGCCTGCATGATATGA**

SEQ ID NO:17

Human T2R09 amino acid sequence

15 MPSAIEAIYIILIAGELTIGIWGNFIVLVNCIDWLKRRDISLIDIILISLAISRICLLC
 VISLDGFFMLLFPPTYGNSVLVSIVNVVWTFANNSSLWFTSCLSIIFYLLKIANISHPFFF
 WLKLKINKVMLAILLGSFLISLIISVPKNDMWYHLFKVSHEENITWKFKVSKI PGTFKQ
 LTLNLGVMVPFILCLISFFLLLFSLVRHTKQIRLHATGFRDPSTEAHMRAIKAVIIFLLL
 20 LIVYYPVFLVMTSSALIPQGKLVLMIGDIVTVIFPSSHFILIMGNSKLRFAFLKMLRFV
 KCFLRRRKPFVP

SEQ ID NO:18

25 Human T2R09 nucleotide sequence

ATGCCAAGTGCAATAGAGGCAATATATATTATTTTAATTGCTGGTGAATTGACCATAGGG
 ATTTGGGGAAATGGATTCATTGTACTAGTTAACTGCATTGACTGGCTCAAAGAAGAGAT
 ATTTCCCTTGATTGACATCATCCTGATCAGCTTGGCCATCTCCAGAATCTGTCTGCTGTGT
 30 GTAATATCATTAGATGGCTTCTTTATGCTGCTCTTTCCAGGTACATATGGCAATAGCGTG
 CTAGTAAGCATTGTGAATGTTGTCTGGACATTTGCCAATAATTCAAGTCTCTGGTTTACT
 TCTTGCCTCAGTATCTTCTATTTACTCAAGATAGCCAATATATCGCACCCATTTTTCTTC
 TGGCTGAAGCTAAAGATCAACAAGGTCATGCTTGCGATTCTTCTGGGGTCCTTTCTTATC
 TCTTTAATTATTAGTGTTCCAAAGAATGATGATATGTGGTATCACCTTTTCAAAGTCAGT

CATGAAGAAAACATTACTTGGAATTCAAAGTGAGTAAATTCCAGGTACTTTCAAACAG
 TTAACCCTGAACCTGGGGGTGATGGTTCCTTTATCCTTTGCCTGATCTCATTCTTTCTTG
 TTACTTTTCTCCCTAGTTAGACACACCAAGCAGATTCGACTGCATGCTACAGGGTTCAGA
 GACCCCAGTACAGAGGCCACATGAGGGCCATAAAGGCAGTGATCATCTTTCTGCTCCTC
 5 CTCATCGTGTACTACCCAGTCTTTCTTGTTATGACCTCTAGCGCTCTGATTCCTCAGGGA
 AAATTAGTGTGATGATTGGTGACATAGTAACTGTCATTTTCCCATCAAGCCATTCATTC
 ATTCTAATTATGGGAAATAGCAAGTTGAGGGAAGCTTTTCTGAAGATGTTAAGATTTGTG
 AAGTGTTTCCTTAGAAGAA**GAAAGCCTTTTGTTCCATAG**

10

SEQ ID NO:19

Human T2R10 amino acid sequence

MLRVVEGIFIFVVVSESVFGVLGNGFIGLVNCIDCAKNKLSTIGFILTGLAISRIFLIWI
 15 IITDGFIIQIFSPNIYASGNLIEYISYFWVIGNQSSMWFATSLSIFYFLKIANFSNYIFLW
 LKSRTNMVLPFMIVFLLISSLLNFAYIAKILNDYKTKNDTVWDLNMYKSEYFIKQILLNL
 GVIFFFTLSLITCIFIILISLWRHNRQMOSNVTGLRDSNTEAHVKAMKVLISFIILFIILYF
 IGMAIEISCFTVRENKLLLMFGMTTTAIYPWGHSFILILGNSKLKQASLRVLQQLKCCEK
 RKNLRVT

20

SEQ ID NO:20

Human T2R10 nucleotide sequence

25 **ATGCTACGTGTAGTGAAG**GCATCTTCATTTTTGTTGTAGTTAGTGAGTCAGTGTTTGGG
 GTTTTGGGGAATGGATTTATTGGACTTGTAAGTGCATTGACTGTGCCAAGAATAAGTTA
 TCTACGATTGGCTTTATTCTCACCGGCTTAGCTATTTCAAGAATTTTCTGATATGGATA
 ATAATTACAGATGGATTTATACAGATATTCTCTCCAAATATATATGCCTCCGGTAACCTA
 ATTGAATATATTAGTTACTTTTGGGTAATTGGTAATCAATCAAGTATGTGGTTTGGCCACC
 30 AGCCTCAGCATCTTCTATTTCTGAAGATAGCAAATTTTCCAACATACATATTTCTCTGG
 TTGAAGAGCAGAACAAATATGGTTCTTCCCTTCATGATAGTATTCTTACTTATTTTCATCG
 TTAATTAATTTTGCATACATTGCGAAGATTCTTAATGATTATAAAACGAAGAATGACACA
 GTCTGGGATCTCAACATGTATAAAAGTGAATACTTTATTAAACAGATTTTGCTAAATCTG
 GGAGTCATTTTCTTCTTTACACTATCCCTAATTACATGTATTTTTTTAATCATTTCCCTT

TGGAGACACAACAGGCAGATGCAATCGAATGTGACAGGATTGAGAGACTCCAACACAGAA
 GCTCATGTGAAGGCAATGAAAGTTTTGATATCTTTCATCATCCTCTTTATCTTGTATTTT
 ATAGGCATGGCCATAGAAATATCATGTTTTACTGTGCGAGAAAACAACTGCTGCTTATG
 TTTGGAATGACAACCACAGCCATCTATCCCTGGGGTCACTCATTTATCTTAATTCTAGGA
 5 AACAGCAAGCTAAAGCAAGCCTCTTTGAGGGTACTGCAGCAATTGAAGTGCTGTGAGAAA
 AGGAAAAATCTCAGAGTCACATAG

SEQ ID NO:21

10 Human T2R11 amino acid sequence

MANMLKNMLTMISAIIDFIMGIQRSRVMLVHCIDWIRRWKLSLIDFILTCWAISRIFXXX
 XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXNHLCT*FATCLAVFYFLKIVNFSYLFYFWLK
 WRINKVAFILPLVSAFSVYQLSFDVHF*CLLVSCPCKYERHMTGLLNVSNNKNVNNIIIF
 15 FIGSLSSFSISSIFFLLLLSS*RHMKHIRFNFRDCRTPVYGPISEPRKRFSFFVLLLYK
 NLPFS

SEQ ID NO:22

20 Human T2R12 amino acid sequence

MSSIWETLFIIRILVV*FIMGTVGN*FIVLVNIID*IRN*KVSLIDFILNCLAISRICFL*
 ITILATSFNIGYEKMPDSKNLAVSFDILWTGSSYFCLSCCTTCLSVFYFLKVANFSNPFL
 WMKWKIHKVLLFIVLEATISFCTTSILKEIIINSLI*ERVTIKGNLTFNYMDTMHDFTS
 25 FLLQMMFILPFVETLASILLILSLWSHTRQMKLHGIYSRDPSTEAHVKPIKAIISFLLL
 FIVHYFISIILTLACPLLDFAARTFSSVLVFFHPSGHSFLLILRDSKLKQASLCVLKKM
 KYAKKDIISHFYKHA

30 **SEQ ID NO:23**

Human T2R12 nucleotide sequence

ATGTCAAGCATTTGGGAGACACTGTTTATAAGAATTCTTGTAGTGTAATTCATAATGGGG
 ACTGTGGGAAATTGATTCATTGTATTGGTTAATATCATTGACTGAATCAGGAACTGAAAG

GTCTCCCTGATTGATTTTATTCTCAACTGCTTGGCCATCTCCAGGATATGTTTCCTGTAG
ATAACAATTTTAGCTACCTCTTTCAATATAGGCTATGAGAAAATGCCTGATTCTAAGAAT
CTTGCAGTAAGTTTGGACATTCTCTGGACAGGATCCAGCTATTTCTGCCTGTCTGTACC
ACTTGCCTCAGTGTCTTCTATTTCTCAAGGTAGCCAACCTTCTCCAATCCCATTTTCCTC
5 TGGATGAAATGGAAAATTCACAAGGTGCTTCTCTTTATTGTACTAGAGGCAACGATCTCT
TTCTGCACAACCTTCCATTCTGAAGGAAATAATAATTAATAGTTTAAATCTAAGAACGGGTA
ACAATAAAAGGCAACTTGACATTTAATTATATGGATACCATGCATGATTTCACTTCTCTG
TTTCTCCTT**CAG**ATGATGTTTCATCCTTCTCTTTGTGGAAACACTGGCTTCCATTCTTCTC
TTAATCCTCTCCTTATGGAGCCACACCAGGCAGATGAAGCTACATGGTATTTATTCCAGG
10 GATCCCAGCACAGAAGCCCATGTAAAACCTATAAAAGCTATAATTTCACTTCTACTCCTC
TTTATTGTGCATTATTTTCATCAGTATCATACTAACATTGGCCTGTCTCTCTAGACTTC
GTTGCGGCAAGGACTTTTAGTAGTGTGCTGGTATTTTCCATCCATCTGGCCATTCATTT
CTTCTAATTTTACGGGACAGCAAACCTGAAGCAAGCTTCTCTCTGTGTCTGAAGAAGATG
AAGTATGCCAAAAGGACATAATCT**CTCATTTTTATAAACATGCCTGA**

15

SEQ ID NO:24

Human T2R13 amino acid sequence

20 MESALPSIFTLVIIAEFIIGNLSNGFIVLINCIDWVSKRELSSVDKLLIILAISRIGLIW
EILVSWFLALHYLAIFVSGTGLRIMIFSWIVSNHFNLWLATIFSIFYLLKIASFSSPAFL
YLKWRVNVKILMILLGTLVFLFLNLIQINMHIKDWLDRIYERNTTWNFMSDFETFSVSVK
FTMTMFSLTPTVAFISFLLLI FSLQKHLQKMQLNYKGRDPRTKVHTNALKIVISFLLF
YASFFLCVLISWISELYQNTVIYMLCETIGVFSPSSH FLLILGNAKLRQAFLLVAAKVW
25 AKR

SEQ ID NO:25

Human T2R13 nucleotide sequence

30

ATGGAAAGTGCCCTGCCGAGTATCTTCACTCTTGTAATAATTGCAGAATTCATAATTGGG
AATTTGAGCAATGGATTTATAGTACTGATCAACTGCATTGACTGGGTCAGTAAAAGAGAG
CTGTCTCAGTCGATAAACTCCTCATTATCTTGGCAATCTCCAGAATTGGGCTGATCTGG
GAAATATTAGTAAGTTGGTTTTTAGCTCTGCATTATCTAGCCATATTTGTGTCTGGAACA

GGATTAAGAATTATGATTTTTAGCTGGATAGTTTCTAATCACTTCAATCTCTGGCTTGCT
 ACAATCTTCAGCATCTTTTATTTGCTCAAAATAGCGAGTTTCTCTAGCCCTGCTTTTCTC
 TATTTGAAGTGGAGAGTAAACAAAGTGATTCTGATGATACTGCTAGGAACCTTGGTCTTC
 TTATTTTTAAATCTGATACAAATAAACATGCATATAAAAGACTGGCTGGACCGATATGAA
 5 AGAAACACAACCTTGAATTTTCAGTATGAGTGACTTTGAAACATTTTCAGTGTCGGTCAAA
 TTCACTATGACTATGTTTCAGTCTAACACCATTTACTGTGGCCTTCATCTCTTTTCTCCTG
 TTAATTTTCTCCCTGCAGAAACATCTCCAGAAAATGCAACTCAATTACAAAGGACACAGA
 GACCCCAGGACCAAGGTCCATACAAATGCCTTGAAAATTGTGATCTCATTCTTTTATTC
 TATGCTAGTTTCTTTCTATGTGTTCTCATATCATGGATTTCTGAGCTGTATCAGAACACA
 10 GTGATCTACATGCTTTGTGAGACGATTGGAGTCTTCTCTCCTTCAAGCCACTCCTTTCTT
 CTGATTCTAGGAAACGCTAAGTTAAGACAGGCCTTTCTTTTGGTGGCAGCTAAG**GGTATGG**
GCTAAACGATGA

15 **SEQ ID NO:26**

Human T2R14 amino acid sequence

MGGVIKSIFTFVLIVEFIIGNLGNSFIALVNCIDWVKGRKISSVDRILTALAI SRISLVW
 LIFGSWCVSVFFPALFATEKMFRLTNIIWTVINHFSVWLATGLGTFYFLKIANFSNSIFL
 20 YLKWRVKKVVLVLLLVT SVFLFLNIALINIHINASINGYRRNKTCSSDSSNFTRFSSLIV
 LTSTVFIFIPFTLSLAMFLLLI FSMWKHRKKMQHTVKISGDASTKAHRGVKSVITFFLLY
 AIFSLSFFISVWT SERLEENLIILSQVMGMAYPSCHSCVLILGNKKLRQASLSVLLWLRY
 MFKDGEPSGHKEFRESS

25

SEQ ID NO:27

Human T2R14 nucleotide sequence

ATGGGTGGTGT CATAAAGAGCATATTTACATT CGTTTTAATTGTGGAATTTATAATTGGA
 30 AATTTAGGAAATAGTTTCATAGCACTGGTGAAGTGTATTGACTGGGTCAAGGGAAGAAAG
 ATCTCTTCGGTTGATCGGATCCTCACTGCTTTGGCAATCTCTCGAATTAGCCTGGTTTGG
 TTAATATTCGGAAGCTGGTGTGTGTCTGTGTTTTTCCCAGCTTTATTTGCCACTGAAAAA
 ATGTTTCAAGATGCTTACTAATATCTGGACAGTGATCAATCATTTTAGTGTCTGGTTAGCT
 ACAGGCCTCGGTACTTTTTATTTTCTCAAGATAGCCAATTTTCTAACTCTATTTTCTC

TACCTAAAGTGGAGGGTTAAAAAGGTGGTTTTGGTGCTGCTTCTTGTGACTTCGGTCTTC
 TTGTTTTTAAATATTGCACTGATAAACATCCATATAAATGCCAGTATCAATGGATACAGA
 AGAAACAAGACTTGCACTTCTGATTCAAGTAACCTTACACGATTTTCCAGTCTTATTGTA
 TTAACCAGCACTGTGTTTATTTTCATACCCTTTACTTTGTCCCTGGCAATGTTTCTTCTC
 5 CTCATCTTCTCCATGTGGAAACATCGCAAGAAGATGCAGCACACTGTCAAAATATCCGGA
 GACGCCAGCACCAAAGCCACAGAGGAGTTAAAAGTGTGATCACTTTCTTCTACTCTAT
 GCCATTTTCTCTCTGTCTTTTTTCATATCAGTTTGGACCTCTGAAAGGTTGGAGGAAAAT
 CTAATTATTCTTTCCCAGGTGATGGGAATGGCTTATCCTTCATGTCACTCATGTGTTCTG
 ATTCTTGGAAACAAGAAGCTGAGACAGGCCTCTCTGTCAGTGCTACTGTGGCTGAGGTAC
 10 ATGTTCAAAGATGGGGAGCCCTCAGGTCACAAAG**GAATTTAGAGAATCATCTTGA**

SEQ ID NO:28

Human T2R15 amino acid sequence

15 MITFLPIIFSILVVVTFVLGNFANGFIVLVNSIEWVKRQKISFADQILTAIVSRVGLLW
 VILLHWYATVLNPGSYSLGVRITTINAWAVTNHFSIWVATSLSIFYFLKIANFSNFIFLH
 LKRRIKSVIPVILLGSLFLVCHLVVNMDSESMWTKEYEGNVSWEIKLSDPHTLSDMTVT
 TLANLIPFTLSLLSFLLLICSLCKHLKMQFHGKGSPPSNTKVHIKALQTVTSFLLLFV
 20 YFLSLITSIWNFRRL*NEPVLMLSQTTAIIYPSFHSFILIWGSKKLKQTFLLILCQIKC

SEQ ID NO:29

Human T2R15 nucleotide sequence

25 **ATGATAACTTTTCTACCCATC**ATTTTTTCCATTCTAGTAGTGGTTACATTTGTTCTTGGG
 AATTTTGCTAATGGCTTCATAGTGTTGGTAAATTCCATTGAGTGGGTCAAGAGACAAAAG
 ATCTCCTTTGCTGACCAAATTCTCACTGCTCTGGCAGTCTCCAGAGTTGGTTTGCTCTGG
 GTAATATTATTACATTGGTATGCAACTGTTTTGAATCCAGGTTATATAGTTTAGGAGTA
 30 AGAATTACTACTATTAATGCCTGGGCTGTAACCAACCATTTAGCATCTGGGTTGCTACT
 AGCCTCAGCATATTTTATTTCTCAAGATTGCCAATTTCTCCAACCTTTATTTTCTTCAC
 TAAAAAGGAGAATTAAGAGTGTCATTCCAGTGATACTATTGGGGTCTTTGTTATTTTGG
 GTTTGTCATCTTGTTGTGGTAAACATGGATGAGAGTATGTGGACAAAAGAATATGAAGGA
 AACGTGAGTTGGGAGATCAAATTGAGTGATCCGACGCACCTTTAGATATGACTGTAACC

CTAACCATACTCATCACCATTATAGGTACTCTATTTGATAAGAGATGTTGGTTATGGGTC
TGGGAAGCTTTTGTCTATGCTTTCATCTTAATGCATTCCACTTCACTGATGCTGAGCAGC
CCTACGTTGAAAAG**GATTCTAAAGGGAAAGTGCTAG**

5

SEQ ID NO:32

Human T2R17 amino acid sequence

MCSAXLLIILSILVVFAFVLGNVANGFIALINVNDWVKTQKISSTDQIVTALAFAFSRIGLL
10 XTLLIILLHWYATVFNSALYSLEVRIVPSNVSAIINHFSIWLATSLSIFYLFKIANFNSNFI
FLHLKKRIKSVLLVILLGSLVFLICNLAVVTMDDSVWTKEFEGNVTWKIELRNAIHLSNM
TITNHASKLHTVHSDSNIFSAVSLEFSXTMLANFTLFIITLISFLLLVCSPCKHLKMMQLH
GKGSQDLSTKVHIKPLQTVISFRMLFAIYFLCIITSTWNPRTQQSNLVFLLYQTLAIMYP
SFHSFILIMRSRKLKQTSLSVLCQVTCWVK

15

SEQ ID NO:33

Human T2R18 amino acid sequence

MFVGINIFFLVVATRGLVLGMLGNGLIGLVNCIEWAKSWKVSSADFILTSLAIVRIIRLY
20 LILFDSFIMVLSPHLYTIRKLVKLFITLWALINQLSI*FATCLSIIFYLLKIANFSHSLFL
WLKWRMNGMIVMLLILSLFLLIFDSLVL EIFIDISLNIIDKSNLTLYLDESKTLYDKLSI
LKTLLSLTYVIPFLLTLTSLLLLFI SLVRHTKNLQLNSLGSRDSSTEAHKRAMKMVIAFL
LLFIINFISTLIGDWIFLEVENYQVMFMILLAFPSGHSFIIILGNKLRQSSLRLW
25 HLKFSCLKKAKPLTS

SEQ ID NO:34

Human T2R18 nucleotide sequence

30

ATGTTTCGTTGGAATTAATATTTTCTTTCTGGTGGTGGCAACAAGAGGACTTGTCTTAGGA
ATGCTGGGAAACGGGCTCATTGGACTGGTAAACTGCATTGAGTGGGCCAAGAGTTGGAAG
GTCTCATCAGCTGATTTTCATCCTCACCAGCTTGGCTATAGTCAGAATCATTCGACTGTAT
TTAATACTATTTGATTCATTTATAATGGTATTGTCCCCTCATCTATATACCATCCGTAAA

CTAGTAAACTGTTTACTATTCTTTGGGCATTAATTAATCAGTTAAGTATCTAGTTTGCC
 ACCTGCCTAAGCATTTTCTACTTGCTTAAGATAGCCAATTTCTCCCACTCCCTTTTCCTC
 TGGCTGAAGTGGAGAATGAACGGAATGATTGTTATGCTTCTTATATTGTCTTTGTTCTTA
 CTGATTTTGGACAGTTTAGTGCTAGAAATATTTATTGATATCTCACTCAATATAATAGAT
 5 AAAAGTAATCTGACTTTATATTTAGATGAAAGTAAACTCTCTATGATAAACTCTCTATT
 TTAAAACTCTTCTCAGCTTGACATACGTTATTCCTTTCTTCTGACTCTGACCTCTTTG
 CTCCTTTTATTTATATCCTTAGTGAGACACACCAAGAATTTGCAGCTCAACTCTCTGGGC
 TCAAGGGACTCCAGCACAGAGGCCCATAAAAGGGCCATGAAAATGGTGATAGCCTTCCTC
 CTCCTTTTTATTATTAACCTTTATTTCCACTTTAATAGGAGATTGGATCTTCCTTGAGGTA
 10 GAGAATTATCAGGTCATGATGTTTATTATGATGATTTTACTTGCCTTTCCTCAGGCCAC
 TCATTTATTATAATTTTGGGAAACAACAAGCTAAGACAGAGCTCCTTGAGACTACTGTGG
 CATCTTAAATTCTCTCTGAAAAAGCAAACCTTTAACTTCATAG

15 **SEQ ID NO:35**

Human T2R19 amino acid sequence

VTTLANLIPFTLSLICFLLLICSLCKHLKKMRLHSGKSQDPSTKVHIKALQTVTSFLMLF
 AIYFLCIITSTWNLRTOQSKLVLLCQTVAIMYPSFHSFILIMGSRKLKQTFLSVLWQMT
 20 C

SEQ ID NO:36

Human T2R19 nucleotide sequence

25 CTGTAACACTCTAGCAAACCTCATACCCTTTACTCTGAGCCTAATATGTTTTCTGCTGT
 TAATCTGTTCTCTTTGTAAACATCTCAAGAAGATGCGGCTCCATAGCAAAGGATCTCAAG
 ATCCCAGCACCAAGGTCCATATAAAAGCTTTGCAAACCTGTGACCTCCTTCCTCATGTTAT
 TTGCCATTTACTTTCTGTGTATAATCACATCAACTTGGAATCTTAGGACACAGCAGAGCA
 30 AACTTGTAACCTGCTTTGCCAAACTGTTGCAATCATGTATCCTTCATTCCACTCATTC
 TCCTGATTATGGGAAGTAGGAAGCTAAAACAGACCTTTCTTTTCAGTTTTGTGGCAGATGA
 CATGCTGAGTGAAAGAAGAGAAACCCTCAACTCCATAGATTCACAAGGGGAGCATCGTGG
 GTCTTCTAGCAGAAAACAACTGATGGTGTCTGGAACATTTTATAT

SEQ ID NO:37

Human T2R20 amino acid sequence

5 HLXRKAKSVVLVIVLGSLFFLVLCQLVMKNTYINVWTEECEGNVTWKIKLRNAMHLSNLT
V
AMLANLIPFTLTVISFLLLIYSLCKHLKKMQLHGKGSQDPSTKIHIALQTVTSFLVLLA
IYFLCLIIS

10 **SEQ ID NO:38**

Human T2R20 nucleotide sequence

TTCATCACTTANAAAGGAAGGCTAAGAGTGTAGTTCTGGTGATAGTGTTGGGGTCTTTGT
TCTTTTTGGTTTGTCAACTTGTGATGAAAAACACGTATATAAATGTGTGGACAGAAGAAT
15 GTGAAGGAAACGTAACCTTGAAGATCAAACCTGAGGAATGCAATGCACCTTTCCAACCTGA
CTGTAGCCATGCTAGCAAACCTGATAACCATTCACCTCTGACCGTGATATCTTTTCTGCTGT
TAATCTACTCTCTGTGTAAACATCTGAAGAAGATGCAGCTCCATGGCAAAGGATCTCAAG
ATCCCAGCACCAAGATCCACATAAAAGCTCTGCAAACCTGTGACCTCCTTCCTCGTATTAC
TTGCCATTTACTTTCTGTGTCTAATCATATCCTTTTG

20

SEQ ID NO:39

Human T2R21 amino acid sequence

25 MPPGIGNTFLIVMMGEFII*MLGNGFIVLVNCIDW*GVK*SY*TTASSPAWLSPQSVNFG
*YYLIHL*QHYGHIYMPSIN**NLFIFFGH*PIT*LPGLLP*CFLLL*NTYFSHPCFIWL
RWRISRTLLELPLGSLLLLFFNLALTGGLSDLWINIYTIYERNSTWSLDVSKILYCSLWI
LVSLIY LISFLLSLISLLLLILSLMRHIRNLQLNTMGPRDLRMKAHKRAMKMKMMVVSF
LLFFLVHFSSLLPTGWIFLIQOK*QANFFVLLTSIIFPSSHSEFVLILENCKLRQTAVGPL
30 WHLKCHLKRVKL

SEQ ID NO:40

Human T2R22 amino acid sequence

MATESDTNLLILAI AEFIISMLGNVFIGLVNCSEXIKNXKVFSADFILTCLAISHNGQLL
VILFDSFLVGLASHLYTTYRLXKNCIMLWT

5

SEQ ID NO:41

Human T2R22 nucleotide sequence

TATAGGGACN**GTGATGCTTCGTACACTCTC**CAAGAAGAAACACTCCGTGAGGTATGTGAG
10 ACTGCATNCCTTAGTAGATCTNTTGGGATATATATTCATAATATAGAAAAANAGGCAAAG
ACTTNCTTAAGTATATGAGACTCTATCCAACAGCAGAAGGTTCTGATCAAGACTGGAAGT
GCAATANAAGCAATGAAGATAAGTATCAGATATGAATGCTCTTCTGCAATGGTCTGATTG
TNACATTATTAATGATACANAGTATTA AAAA ACTTGGATTTTNTTGTCTCTGGAGATGGCC
ACCGAATCGGACACAAATCTTCTGATTCTGGCAATAGCAGAATTCATCATCAGCATGCTG
15 GGAATGTGTTCAATTGGACTGGTAAACTGCTCTGAANGGATCAAGAACCANAAGGTCTTC
TCAGCTGACTTCATCCTCACCTGCTTGGCTATCTCTCACAATGGACA ACTGTTGGTGATA
CTGTTTGATTCA TTTCTAGTGGGACTTGCTTCACATCTATATAACCACATATAGACTANGA
AAAAACTGTATTATGCTTTGGACATGACTAATCACTTGACACACTGCTTCGCACGTGCTA
GCATATTCTATTCTTAGATAGCCACTTCNCACTCCTT**GTCTCTGCTGAAGTGGGAT**

20

SEQ ID NO:42

Human T2R23 amino acid sequence

25 VAFVLGNVANGFIALVNVIDXVNTRKISSAEQILTALVVS RIGXTLXHSIP*DATRC*SA
LYRXEVRIVASN

SEQ ID NO:43

30 Human T2R23 nucleotide sequence

AGGGTTGAGTCGTGCTTATCTTCACTTAACCTAGTATANAANTACAGCATATAGCAAGGA
GAGAATGTATATGAAGAGGAGTGAATTTGAGTCTGTTTGAGAATAATGACCTTTTCTATT
TCTATAAAGACAGTTTTGAATTCATCTATTAGCATATGCTGGTGCTTGCCGTGTGACACT

AGTCACTGAATTTAAAGGCAGAAAATGTTATTGCACATTTAGTAATCAAGTGTTTCATCGA
AGTTAACATCTGGATGTTAAAGGACTCAGAACAAGTGTTACTAAGCCTGCATTTTTTTAT
CTGTTCAAACATGATGTGTTNTCTGCTCATCATTTTCATCAATTCTGGTAGAGTTGCATTT
GTTCTTGGAATGTNGCCAATGGCTTCATAGCTCTAGTAAATGTCATTGACTGNGTTAAC
5 ACACGAAAGATCTCCTCAGCTGAGCAAATTCTCACTGCTCTGGTGGTCTCCAGAATTGGT
NNTACTCTGNGTCATAGTATTCCTTGAGATGCAACTAGATGTTAATCTGCTCTATATAGG
NTAGAAGTAAGAATTGTTGCTTCTAATGCCTGAGCTCGTACGAACCATT

10 **SEQ ID NO:44**

Human T2R24 amino acid sequence

MATELDKIFLILAIAEFIISMLGNVFIGLVNCSEGIKNQKVFSADFILTCLAISTIGQLL
VILFDSFLVGLASHLYTTYRLGKTVIMLWHMTNHLTTWLATCLSIIFYFFKIAHFPHSLFL
15 WLRWRMNGMIVMLLILSLFLLIFDSLVL EIFIDISLNIIDKSNLTLYLDESKTLYDKLSI
LKTLLSLTSFIPFSLFLTSLFLFLSLVRHTRNLKLSSLGSRDSSTEAHRRAMKMVMSFL
FLFIVHFFSLQVANGIFFMLWNNKYIKFVMLALNAFPSCHSFILILGNSKLRQTAVRLLW
HLRNYTKTPNALPL

20

SEQ ID NO:45

Human T2R24 nucleotide sequence

ATGGCCACCGAATTGGACAAAATCTTTCTGATTCTGGCAATAGCAGAATTCATCATCAGC
25 ATGCTGGGGAATGTGTTTCATTGGACTGGTAAACTGCTCTGAAGGGATCAAGAACCAAAAG
GTCTTCTCAGCTGACTTCATCCTCACCTGCTTGGCTATCTCCACAATTGGACAACCTGTTG
GTGATACTGTTTGATTTCATTTCTAGTGGGACTTGCTTCACATTTATATACCACATATAGA
CTAGGAAAACTGTTATTATGCTTTGGCACATGACTAATCACTTGACAACCTGGCTTGCC
ACCTGCCTAAGCATTTTCTATTTCTTTAAGATAGCCCACTTCCCCCACTCCCTTTTCTC
30 TGGCTGAGGTGGAGGATGAACGGAATGATTGTTATGCTTCTTATATTGTCTTTGTTCTTA
CTGATTTTTTGACAGTTTAGTGCTAGAAATATTTATTGATATCTCACTCAATATAATAGAT
AAAAGTAATCTGACTTTATATTTAGATGAAAGTAAACTCTCTATGATAAACTCTCTATT
TTAAAACTCTTCTCAGCTTAACCAGTTTTATCCCCTTTTCTCTGTTCTGACCTCCTTG
CTTTTTTTATTTCTGTCCTTGGTGAGACATACTAGAAATTTGAAGCTCAGTTCCTTGGGC

TCTAGAGACTCCAGCACAGAGGCCCATAGGAGGGCCATGAAAATGGTGATGTCTTTCCTT
TTCCTCTTCATAGTTCATTTTTTTTCCTTACAAGTGGCCAATGGGATATTTTTTATGTTG
TGGAACAACAAGTACATAAAGTTTGTCATGTTAGCCTTAAATGCCTTTCCTCGTGCCAC
TCATTTATTCTCATTTCTGGGAAACAGCAAGCTGCGACAGACAGCTGTGAGGCTACTGTGG
5 CATCTTAGGAACTATACAAAAACACCAAATGCTTTACCTTTGTAG

SEQ ID NO:46

Human T2R25 amino acid sequence

10

LSPFRMLFAIYFLCIITSTWNPRTQQSNLVFLLYQTLAIMYPSFHSFILIMRSRKLKQTS
LSVLCQVTCWVK

SEQ ID NO:47

Human T2R26 amino acid sequence

15

MPPGIGNTFLIVMMGEFII*MLGNGFIVLVNCIDVRSQMILLDNCILTSLAISTISQLWI
ILLDSFVTALWPHLYAFNKLIKFIHIFWALTNHLVTWLACCLSVFYFFKIAFYFSHPCFIW
20 LRWRISRTLLELPLGSLLLLLFFNLALTGGLSDLWINIYTMYERNSTWSLDVSKILYCSLW
ILVSLIYLISFLLSLISLLLLILSLMRHIRNLQLNTMGPRDLRMKAHKRAMKMKMKMMVS
FLLFFLVHFSSLLPTGWIFLIQOK

SEQ ID NO:48

Human T2R27 amino acid sequence

25

30

LANLIDWAENQICLMDFILSSLAICRTLTLGCCVAIRCTYNDYPNIDAVNHNLIKIITIF
DILRLVSK*LGIWFASYLSIFYLLKVALFHHAIFLWLKWRISRAVFTFLMIFLFFYISII
SMIKIKFLDQC*YKI*EKLLLEGRCE*SPPSC*PDAH*PGVVYSLYHFSYLMFLVCYLP
KGKHCTAVVIGDWLQRPRTAYVRAMNIMIAFFHLLYSLGTSLSVSYFLCKRKIVALG
AYLSYPLSHSFILIMENNKVRKAL

SEQ ID NO:49

Human T2R28 amino acid sequence

NICVLLIILSILVVSAFVLGNVANGFIALINVNDW

5

SEQ ID NO:50

Human T2R29 amino acid sequence

10 MQAALTAFVLLFSLLSLLGIAANGFIVLVLGKEWL

SEQ ID NO:51

Human T2R30 amino acid sequence

15

MITFLPIIFSILVVTFVLGNFNSNGFIALVNSIEWVKTRKISSADQILTALVVS RVGLLW
VILLHWYANVFENSALYSSEVGAVASNISAIINHFSIWLATSLSIFYLLKIANFSNLI FLH
LKKRIRSVVLVILLGPLVFLICNLAVITMDDSVWTKEYEGNVTWKIKLRNAIHLSNMTVS
TLANLIPFILTLICFLLLLICSLCKHLKMQHLHGKGSQDPSTKVHIKALQTVTSFLLLCAI
20 YFLSMIISVCNFRLEKQPVFMFCQAIIFSYPSTHPFILILGNKKLKQIFLSVLRHVRYW
VKDRSLRLHRFTRGALCVF

SEQ ID NO:52

25 Human T2R30 nucleotide sequence

ATGATAACTTTTCTACCCATCATTTTTTCCATTCTGGTAGTGGTTACATTTGTTCTTGGA
AATTTTCCAATGGCTTCATAGCTCTAGTAAATTCCATTGAGTGGGTCAAGACACGAAAG
ATCTCCTCAGCTGACCAAATCCTCACTGCTCTGGTGGTCTCCAGAGTTGGTTTACTCTGG
30 GTCATATTATTACATTGGTATGCAAATGTGTTTAATTCAGCTTTATATAGTTCAGAAAGTA
GGAGCTGTTGCTTCTAATATCTCAGCAATAATCAACCATTTCAGCATCTGGCTTGCTACT
AGCCTCAGCATATTTTATTTGCTCAAGATTGCCAATTTCTCCAACCTTATTTTTCTCCAC
TTAAAGAAGAGAATTAGGAGTGTTGTTCTGGTGATACTGTTGGGTCCCTTGGTATTTTTG
ATTTGTAATCTTGCTGTGATAACCATGGATGACAGTGTGTGGACAAAAGAATATGAAGGA

AATGTGACTTGGAAGATCAAATTGAGGAATGCAATACACCTTTCAAATATGACTGTAAGC
 AACTAGCAAACCTCATACCCTTCATTCTGACCCTAATATGTTTTCTGCTGTTAATCTGT
 TCTCTGTGTAAACATCTCAAGAAGATGCAGCTCCATGGCAAAGGATCTCAAGATCCCAGC
 ACCAAGGTCCACATAAAAGCTTTGCAAACGTGACCTCCTTTCTTCTGTTATGTGCCATT
 5 TACTTTCTGTCCATGATCATATCAGTTTGTAAATTTGGGAGGCTGGAAAAGCAACCTGTC
 TTCATGTTCTGCCAAGCTATTATATTCAGCTATCCTTCAACCCACCCATTCATCCTGATT
 TTGGGAAACAAGAAGCTAAAGCAGATTTTTCTTTCAGTTTTGCGGCATGTGAGGTACTGG
 GTGAAAGACAGAAGCCTTCGTCTCCATAGATTACAAAGAGGGGCATTGTGTGTCTTCTAG

10

SEQ ID NO:53

Human T2R31 amino acid sequence

15

MTTFIPIIFSSVVVLFVIGNFANGFIALVNSIERVKRQKISFADQILTALAVSRVGLLW
 VLLLNWYSTVFENPAFYSEVVRTTAYNVWAVTGHFSNWLATSLSIFYLLKIANFSNLI FLH
 LKRRVKSIVLVMLLGPLLFLACQLFVINMKEIVRTKEFEGNMTWKIKLKSAMYFSXMTVT
 IGAXLVPFTLSLISFLMLICSLCKHLKKMQLHGEQSQDLSTKVHIKALQTLISFLLLCAI
 FFLFLIVSVWSPRRLRNDPVMVSKAVGNIYLA FDSFILIWR TKKLKHTFLLILCQIRC

20

SEQ ID NO:54

Human T2R31 nucleotide sequence

25

ATGACAACCTTTTATACCCATCATTTTTTCCAGTGTGGTAGTGGTTCTATTTGTTATTGGA
 AATTTTGCTAATGGCTTCATAGCATTGGTAAATTCCATTGAGCGGGTCAAGAGACAAAAG
 ATCTCTTTTGCTGACCAGATTCTCACTGCTCTGGCGGTCTCCAGAGTTGGTTGCTCTGG
 GTATTATTATTAAATTGGTATTCAACTGTGTTTAATCCAGCTTTTTATAGTGTAGAAGTA
 AGAACTACTGCTTATAATGTCTGGGCAGTAACCGGCCATTTCAAGCAACTGGCTTGCTACT
 AGCCTCAGCATATTTTATTTGCTCAAGATTGCCAATTTCTCCAACCTTATTTTTCTTCAC
 30 TTAAAGAGGAGAGTTAAGAGTGTCAATTCTGGTGATGCTGTTGGGGCCTTTACTATTTTGTG
 GCTTGTCAACTTTTTGTGATAAACATGAAAGAGATTGTACGGACAAAAGAATTTGAAGGA
 AACATGACTTGGAAGATCAAATTGAAGAGTGCAATGTACTTTTCANATATGACTGTAACC
 ATTGGAGCANACTTAGTACCCTTTACTCTGTCCCTGATATCTTTTCTGATGCTAATCTGT
 TCTCTGTGTAAACATCTCAAGAAGATGCAGCTCCATGGAGAAGGATCGCAAGATCTCAGC

ACCAAGGTCCACATAAAAGCTTTGCAAACCTCTGATCTCCTTCCTCTTGTTATGTGCCATT
TTCTTTCTATTCCCTAATCGTTTCGGTTTGGAGTCCTAGGAGGCTGCGGAATGACCCGGTT
GTCATGGTTAGCAAGGCTGTTGGAAACATATATCTTGCATTGCGACTCATTCATCCTAATT
TGGAGAACCAAGAAGCTAAAACACACCTTTCTTTTGATTTTGTGTCAGATTAGGTGCTGA

5

SEQ ID NO:55

Human T2R32 amino acid sequence

10 HSFMLTMGSRKPKQTFLSAL

SEQ ID NO:56

Human T2R33 amino acid sequence

15

MVYFLPIIFSILVVFAFVLGNFSGFIALVNVIDWVKRQKISSADQILTALVVS RVGLLW
VILLHWYANVFNSALYSLEVRIVASNISAVINHFSIWLAASLSIFYLLKIANFSNLIFLH
LKKRIKSVVLVILLGPLVFLICNLAVITMDERVWTKEYEGNVTWKIKLRNAIHLSSLTVT
TLANLIPFTLSLICFLLLICSLCKHLKMQLSHSGSQDPSTKVHIKALQTVISFLMLCAI
20 YFLSIMISVWNLRSLNKPVFMFCKAIRFSYPSIHPFILIWGNKKLKQTFLSVFWQVRYW
VKGEKPSSP

SEQ ID NO:57

25 Human T2R33 nucleotide sequence

ATGGTATATTTTCTGCCCATCATTTTTTCCATTCTGGTAGTGTTTGCATTTGTTCTTGGA
AATTTTTCCAATGGCTTCATAGCTCTAGTAAATGTCATTGACTGGGTAAAGAGACAAAAG
ATCTCCTCAGCTGACCAAATTCTCACTGCTCTGGTGGTCTCCAGAGTTGGTTTACTCTGG
30 GTCATATTATTACATTGGTATGCAAATGTGTTTAATTCAGCTTTATATAGTTTAGAAGTA
AGAATTGTTGCTTCTAATATCTCAGCAGTAATCAACCATTTTCAGCATCTGGCTTGCTGCT
AGCCTCAGCATATTTTATTTGCTCAAGATTGCCAATTTCTCCAACCTTATTTTTCTCCAC
CTAAAGAAGAGAATTAAGAGTGTTGTTCTGGTGATACTGTTGGGGCCCTTGGTATTTCTG
ATTTGTAATCTTGCTGTGATAACCATGGATGAGAGAGTGTGGACAAAAGAATATGAAGGA

AATGTGACTTGGAAGATCAAATTGAGGAATGCAATACACCTTCAAGCTTGACTGTA
 ACTCTAGCAAACCTCATACCCTTTACTCTGAGCCTAATATGTTTTCTGCTGTTAATCTGT
 TCTCTTTGTAAACATCTCAAGAAGATGCAGCTCCATAGCAAAGGATCTCAAGATCCCAGC
 ACCAAGGTCCACATAAAAGCTTTGCAAACCTGTGATCTCCTTCCTCATGTTATGTGCCATT
 5 TACTTTCTGTCCATAATGATATCAGTTTGGAACTCTTAGGAGTCTGGAAAACAAACCTGTC
 TTCATGTTCTGCAAAGCTATTAGATTGAGCTATCCTTCAATCCACCCATTCATCCTGATT
 TGGGGAAACAAGAAGCTAAAGCAGACTTTTCTTTTCTTTTGGCAAGTGAGGTACTGG
 GTGAAAGGAGAGAAGCCTTCATCTCCATAG

10

SEQ ID NO:58

Human T2R34 amino acid sequence

GSSRXKPPRI PHKKLCKLGPSFPHNNLPIYFLCXNHIVLEFLKMRPKKKCSLMLCQAFGI
 15 IYPSFHSFILXWGNKTLKQTFLSVXWQVTCWAKGQNQSTP

SEQ ID NO:59

Human T2R35 amino acid sequence

20

NAIRPSKLWTVTEADKTSQPGTSANKIFSAGNLISHVNMSRRMQLHGKGSQHLSTRVHIK
 AXQTVISFLMLXAIYFLCLITSTWNPRTQQSKLVFLLYQTLGFMYLLFHSFILTMGSRKP
 KQTFLSAL

25

SEQ ID NO:60

Human T2R36 amino acid sequence

MICFLLIILSILVVFAFVLGNFSNGFIALVNVIDWVKRQKISSADQILTALVVS RVGLLW
 30 VILLHWYSNVLNSALYSSEVIIIFISNAWAIINHFSIWLATSLSIFYLLKIVNFSRLIFHH
 LKRKAKSVVLVIVLGPLVFLVCHLVMKHTYINVWTKKEYEGNVTKIKLRNAIHLSNLTVS
 TLANLIPFTLTLSIFLLLIYSLCKHLKKMQLHGKGSQDPSTKVHIKALQTVTSFLLLCAI
 YFLSMIISVCNFGRLKQPVFMFCQAIIFSYPSTHPFILILGNKKLKQIFLSVFWQMRYW
 VKGEKPSSP

SEQ ID NO:61

Human T2R36 nucleotide sequence

5
 ATGATATGTTTTCTGCTCATCATTTTATCAATTCTGGTAGTGTTTGCATTTGTTCTTGGA
 AATTTTTCCAATGGCTTCATAGCTCTAGTAAATGTCATTGACTGGGTCAAGAGACAAAAG
 ATCTCCTCAGCTGACCAAATCCTCACTGCTCTGGTGGTCTCCAGAGTTGGTTTACTCTGG
 GTAATATTATTACATTGGTATTCAAATGTGTTGAATTCAGCTTTATATAGTTCAGAAGTA
 10 ATAATTTTTATTTCTAATGCCTGGGCAATAATCAACCATTTTCAAGCATCTGGCTTGCTACT
 AGCCTCAGCATATTTTATTTGCTCAAGATCGTCAATTTCTCCAGACTTATTTTTTCATCAC
 TTAAAAGGAAGGCTAAGAGTGTAGTTCTGGTGATAGTGTTGGGTCCCTTGGTATTTTTG
 GTTTGTCACCTTGTGATGAAACACACGTATATAAATGTGTGGACAAAAGAATATGAAGGA
 AATGTGACTTGGAAGATCAAACCTGAGGAATGCAATACACCTTTCAAACCTTGACTGTAAGC
 15 AACTAGCAAACCTTGATACCCTTCACTCTGACCCTGATATCTTTTCTGCTGTTAATCTAC
 TCTCTGTGTAAACATCTCAAGAAGATGCAGCTCCATGGCAAAGGATCTCAAGATCCCAGC
 ACCAAGGTCCACATAAAAGCTTTGCAAACCTGTGACCTCCTTTCTTCTGTTATGTGCCATT
 TACTTTCTGTCCATGATCATATCAGTTTGTAAATTTTGGGAGGCTGGAAAAGCAACCTGTC
 TTCATGTTCTGCCAAGCTATTATATTCAGCTATCCTTCAACCCACCCATTCATCCTGATT
 20 TTGGGAAACAAGAAGCTAAAGCAGATTTTTCTTTTCAAGTTTGGCAAATGAGGTACTGG
 GTGAAAGGAGAGAAGCCTTCATCTCCATAG

SEQ ID NO:62

25 Human T2R37 amino acid sequence

MITFLPIIFSILIVVTFVIGNFANGFIALVNSIEWVKRQKISSADQISHCSGGVQNWFTL
 GHIITLVCNCV*FGFI*IRSKNFWF*CLSNNAFQHVGVTSLSIFHLLKTANFSNLIFLH
 LKKRIKSVGLVILLGPLLFFICNLFVINMDES VWTKKEYEGNVTKIKLRSAMYHSNMTLT
 30 MLANFVPFTLTLISFLLLICSLCKHLKMKQLHGKGSQDPSTKVHIKALQTVTSFLLLCAI
 YFLSMIISVCNLRLEKQPVFMFCEAIIFSYPSTHPFILILGNKKLKQIFLSVLRHVRYW
 VKGEKPSSS

SEQ ID NO:63

Human T2R37 nucleotide sequence

ATGATAACTTTTCTGCCCATCATTTTTTCCATTCTAATAGTGGTTACATTTGTGATTGGA
5 AATTTTGCTAATGGCTTCATAGCTCTAGTAAATTCCATTGAGTGGGTAAAGAGACAAAAG
ATCTCATCAGCTGACCAAATTTCTCACTGCTCTGGTGGTGTCCAGAATTGGTTTACTCTG
GGTCATATTATTACATTGGTATGCAACTGTGTTTAATTTGGCTTCATATAGATTAGAAGT
AAGAATTTTTGGTTCTAATGTCTCAGCAATAACCAAGCATTTCAGCATGTGGGTGTTACT
AGCCTCAGCATATTTCAATTTGCTCAAGACTGCCAATTTCTCCAACCTTATTTTTCTCCAC
10 CTAAAGAAGAGGATTAAGAGTGTTGGTTTGGTGATACTATTGGGGCCTTTGCTATTTTTC
ATTTGTAATCTTTTTGTGATAAACATGGATGAGAGTGTATGGACAAAAGAATATGAAGGA
AACGTGACTTGGAAGATCAAATTGAGGAGTGCAATGTACCATTCAAATATGACTCTAACC
ATGCTAGCAAACCTTTGTACCCTTCACTCTGACCCTGATATCTTTTCTGCTGTTAATCTGT
TCTCTGTGTAAACATCTCAAGAAGATGCAGCTCCATGGCAAAGGATCTCAAGATCCCAGC
15 ACCAAGGTCCACATAAAAGCTTTGCAAACCTGTGACCTCCTTTCTTCTGTTATGTGCCATT
TACTTTCTGTCCATGATCATATCAGTTTGTAATTTGGGGAGGCTGGAAAAGCAACCTGTC
TTCATGTTCTGCGAAGCTATTATATTCAGCTATCCTTCAACCCACCCATTCATCCTGATT
TTGGGAAACAAGAAGCTAAAGCAGATTTTCTTTTCAGTTTTCGCGCATGTGAGGTACTGG
GTGAAAGGAGAGAAGCCTTCATCTTCATAG

20

SEQ ID NO:64

Human T2R38 amino acid sequence

25 MLTLTRIRTVSYEVRSTFLFISVLEFAVGFLTNAFVFLVNFWDVVKRQPLSNSDCVLLCL
SISRLFLHGLLFLSAIQLTHFQKLSEPLNHSYQAIIMLWMIANQLNLWLAACLSLLYCSK
LIRFSHTFLICLASWSPGRSPVPS

30 **SEQ ID NO:65**

Human T2R39 amino acid sequence

LRNAGLNDSTNAKLVRNNDLLLINLILLLPLSVFVMCTSMFLVSLYKMHWMQSESHKLSS
ARTEAHINALKTVTTFFCFFVSYFAAFMANMTFRIPYRSHQFFVVKEIMAAYPAGHSVII
VLSNSKFKDLFRMICLQKE

5

SEQ ID NO:66

Human T2R40 amino acid sequence

10 SQYSLGHSYVVIFGYGQMKKTFILGILWHLKCGLKGRALLATQVGLREKSTRSLGVIFLAS
SYSFFVYVLCH

SEQ ID NO:67

Human T2R41 amino acid sequence

15

MITFLLIILSILVVFAFVLGNFNSNGFIALVNVIDWVNTRKISSADQILTALAVSRVGLLW
VILLHWYANVLNPALYSSEVIIIFISNISAIINHFSIWLATSLSIFYLLKIVNFSRLIFHH
LKRKAQSVVLVIVLGPLVFLVCHLVMKHTYINVWTKEYEGNVTWKIKLRNATHLSNLTVS
TLANLIPFTLTLLISFLLLICSLCKHLKMQHLSKGSQDPSTKVHIKALQTVTSFLMLFAI
20 YFLYLITSTWNL*TQQSKLVFMFCQTLGIMYPSFHSFILIMGSRKLKQTFLSVLCQVTCL
VKGQQPSTP

SEQ ID NO:68

25 Human T2R42 amino acid sequence

FIGLTDCIAWMRNQKLCMVGFILTRMALARINIL

30 **SEQ ID NO:69**

Human T2R43 amino acid sequence

LELIFS*KVVATRGLVLGMLGNGLIGLVNCIEWAKSWKVSSADFILTSLAIVRIIRLYLI
LFDSFIMVLSPHLYTXXXXXXXXXXXXXXXXXXXXXXXXXSLSI FHWFKTANFSNLI FLPLK

EED*NVWLGDVAGALGIFHL*SCSENHG*EVCQGQNMKEFCSGMIKLRNAIQLSNLTVTM
PANVTPCTLTTLISFLLLIYSPCKHVKKMQLHGKGSQHLSTKVHIKVLQTVISFFLLCAIY
FVSVIISVWSFKNLENKPVFMFCQAIGFSCSSAHPFILTGMGNKKLKQTYLSVLWQMR

5

SEQ ID NO:70

Human T2R44 amino acid sequence

MITFLPIIFSILIVVIFVIGNFANGFIALVNSIEWVKRQKISFVDQILTALAVSRVGLLW
10 VLLLHWYATQLNPAFYSSVEVRITAYNVWAVTNHFSSWLATSLSMFYLLRIANFSNLIFLR
IKRRVKSIVLVILLGPLLFLVCHLFVINMDETVWTKEYEGNVTWKIKLRSAMYHSNMTLT
MLANFVPLTTLTLISFLLLICSLCKHLKKMQLHGKGSQDPSTKVHIKALQTVTSFLLLCAI
YFLSMIISVCNLGRLEKQPVFMFCQAIIFSYPSTHPFILILGNKKLKQIFLSVLRHVRYW
VKDRSLRLHRFTRGALCVF

15

SEQ ID NO:71

Human T2R45 amino acid sequence

MATELDKIFLILAIAEFIISMLGNVFIGLVNCSEGIKNQKVFSADFILTCLAISTIGQLL
20 VILFDSFLVGLASHLYTTYRLGKTIVIMLWHMTNHLTTWLATCLSIFYFFKIAHFPHSLFL
WLRWRMNGMIVMLLILSLFLLIFDSLVL EIFIDISLNIIDKSNLTLYLDESKTLYDKLSI
LKTLLSLTSFIPFSLFLTSLFLFLSLVRHTRNLKLSSLGSRDSSTEAHRRAMKMVMSFL
FLFIVHFFSLQVANWIFFMLWNNKCIKFVMLALNAFPSCHSFILILGNSKLQQTAVRLLW
25 HLRNYTKTPNPLPL

SEQ ID NO:72

Human T2R46 amino acid sequence

30

MSFLHIVFSILVVAFILGNFANGFIALINFIWVKKQKISSADQIIADKQSPELVCSG

SEQ ID NO:73

Human T2R47 amino acid sequence

MLNALYSILIIIIINI*FLIGILGNGFITLVNGIDWVKM*KRSSILTALTISRICLISVIM
VRWFI

5

SEQ ID NO:74

Human T2R48 amino acid sequence

10 VSRVGLLWVILLHWYSTVLNPTSSNLKVIIIFISNAWAVTNHFSIWLATSLSIFYLLKIVN

SEQ ID NO:75

Human T2R49 amino acid sequence

15

TVTMLANLVPFTVTLISFLLLVC SLCKHLKMMHLHGKGSQDPSTKVHIKVLQTVISFLLL
CAIFYVSVIISS

SEQ ID NO:76

Human T2R50 amino acid sequence

MITFLPIIFSILVVVTFVIGNFANGFIALVNSTEWVKRQKISFADQIVTALA VSRVGLLW
VLLLNWYSTVLNPAFY SVELRTTAYNIWAVTGHFSNWPATSLSIFYLLKIANF SNLI FLR
25 LKRRVKSVILVLLGPLLFLACHLFVVNMNQI VWTKEYEGNMTWKIKLRRAMYLSDTTVT
MLANLVPFTVTLISFLLLVC SLCKHLKMQ LHGKGSQDPSTKVHIKVLQTVISFFLLCAI
YFVSVIISVWSFKNLENKPVFMFCQAIGFSCSSAHPFILIWGNKKLKQTYLSVLWQMRY

SEQ ID NO:77

Rat T2R01 amino acid sequence

MMEGHILFFFLVVMVQFVTGVLANGLIVVHAIDLIMWKKMAPLDLLLFCLATSRIILQL
CILFAQQLCFLSLVRHTLFEDNITFVFIINELSLWFATWLG VFYCAKIATIPHPLFLWLKM

RISRLVPWLILGSVLYVIITTFIHSRETSAILKPIFISLFPKNATQVGTGHATLLSVLVL
GLTLPLFIFTVAVLLLIYSLWNYSRQMRMTVGTREYSGHAHISAMLSILSFLILYL SHYM
VAVLISTQVLYLGSRTFVFCLLVIGMYPsiHSIVLILGNPKLKRNAKMFIVHCKCCHCTR
AWVTSRSPRLSDLPVPPTHPSANKTSCSEACIMPS

5

SEQ ID NO:78

Rat T2R01 nucleotide sequence

10 CAGGAATCATAAATGGCTGAAACTGGGCAGAACTCTATGCATTATTTAAAGAAGTCATTG
GTTTGTCAATTCTTAAAATGATGGAAGGGCATATACTCTTCTTCTTTTGGTTGTGATGGT
GCAGTTTGTCACTGGGGTCTTGGCAAATGGCCTCATTGTGGTTGTCCATGCTATTGACTT
GATCATGTGGAAGAAAATGGCCCCGTGGATCTGCTTCTATTTTGCCTGGCGACTTCTCG
GATCATTCTGCAGTTATGTATATTGTTTGCACAATTGTGTCTATTCTCTTTGGTGAGACA
15 CACTTTATTTGAGGACAATATTACCTTTGTCTTCATCATAAATGAACTGAGTCTTTGGTT
TGCTACATGGCTCGGTGTTTTCTACTGTGCCAAGATTGCTACCATTCCCTACCCACTCTT
TCTGTGGCTGAAGATGAGGATATCCAGGTGGTACCATGGCTGATCCTGGGATCTGTGCT
CTATGTAATTATTACTACTTTTCATCCATAGCAGAGAGACTTCAGCAATCCTTAAACCAAT
TTTTATAAGCCTTTTTCTAAAAATGCAACTCAAGTCGGAACAGGGCATGCCACACTACT
20 CTCAGTCCTGGTCCTTGGGCTCACACTGCCGTTGTTTCATCTTTACTGTTGCTGTTCTGCT
CTTGATATACTCCCTGTGGAATTATAGCAGGCAGATGAGGACTATGGTAGGCACCAGGGA
GTATAGCGGACATGCTCACATCAGTGCAATGCTGTCCATTCTATCATTCCCTCATCCTCTA
TCTCTCCCACTACATGGTGGCTGTTCTGATCTCTACTCAAGTCCTCTACCTTGGGAAGCAG
AACCTTTGTATTCTGCTTACTGGTTATTGGTATGTACCCCTCAATACACTCGATTGTCTT
25 AATTTTAGGAAATCCTAAGCTGAAACGAAATGCAAAAATGTTTCATTGTCCATTGTAAGTG
TTGTCATTGTACAAGAGCTTGGGTCACCTCAAGGAGCCCAAGACTCAGTGACTTGCCAGT
GCCTCCTACTCATCCCTCAGCCAACAAGACATCCTGCTCAGAAGCCTGTATAATGCCATC
CTAATTGTCCAGCCTGAGGTTTAATCCTAGGTTTGGTACTATTTCAAAGAGTAAAGTTGA
TCATTAAAGCACAACATATGTTGGTGGATGACATCAAGGTCCATATCCCAGTTGTCAATT
30 GTAAACCTCACCTTGCAAGATGATGTCACTGAGAAAGCAGGACAAATGGAGTCTAGGTCC
TTCTGTATGACTTGCTGCAGTATATGTGAATCTATAATTTTCTCCAAAAAACAAAAAA
AAAAAA

00220-220156

SEQ ID NO:79

Rat T2R02 amino acid sequence

5 MFSQKTNYSHLFTFSIIFYVEIVTGILGNGFIALVNIMDWLKRRRISTADQILTALALTR
LIYVWSVLICILLFLCPHLSMRPEMFTAIGVIWVDNHFSIWLATCLGVFYFLKIASFS
NSLFLYLKWRVKVVLMIILISLIFLMLNISSLGMYDHFSIDVYEGNMSYNLVDSTHFPR
IFLFTNSSKVFLIANSSHVFLPINSLFMLIPFTVSLVAFFVLFLSLWKHHKKMQVNAKGP
RDASTMAHTKALQIGFSFLLLYAIYLLFIITGILNLDLMRCIVILLEFDHISGAVFSISHS
FVLILGNSKLRQATLSVLPCLRCRSKDMDTVVF

10

SEQ ID NO:80

Rat T2R02 nucleotide sequence

15 ATTTTGCTCCACTATTTTGCTCTTCTGCAGTAACACAGACCACAAAACAATGGAGCCAAT
GGGTCAAGAGCTGAACTTCAGGAAGTGGGAGCCAAATTTTCTTTGTGATAGGTTGGCAT
ATGAGAATTCATTATTTGATGCAGCTTCTGAAACTGGATGTGAAATACTGGATGAAGCA
GAGGTGATGACCCCTTTGAAATTAAAAAGCCAAGATGTTTCATGGAGAAATTATAAAACAA
TATCTGGGAAATTTGATGCTTCCTAATCGGGTGTAATGGGATTTTAAATGATGAACATT
20 TTGAATTTCCAATGACCATTATGTAAAGTTTTTAAACACAGTAGAGACATCATAAATTGA
AGCATGTTCTCACAGAAAACAACTACAGCCATTTGTTTACTTTTTCAATTATTTTTTAT
GTGGAAATAGTAACAGGAATCTTAGGAAATGGATTCATAGCACTAGTGAATATCATGGAC
TGGCTCAAGAGGAGGAGGATCTCTACTGCAGATCAGATTCTCACTGCTTTGGCCCTTACC
AGACTCATTTATGTGTGGTCTGTACTCATTTGTATATTGTTACTATTTCTGTGCCACAT
25 TTGTCTATGAGACCAGAAATGTTTACAGCGATAGGTGTTATCTGGGTAGTGGATAACCAC
TTCAGCATCTGGCTTGCTACATGTCTTGGTGTCTTTTATTTCTCCTCAAATAGCCAGTTTT
TCTAACTCTTTGTTTCTTTACCTAAAGTGGAGAGTTAAAAAAGTGGTTTTAATGATAATA
CTGATATCACTGATTTTCTTGATGTTAAACATTTTCATCATTAGGGATGTATGATCATTTT
TCAATTGATGTTTATGAAGGTAATATGTCTTATAATTTGGTGGATTCAACACATTTTCCC
30 AGAATTTTCTTATTCACAACTCATCTAAGGTCTTCTTAATCGCCAATTCATCCCATGTT
TTCTTACCCATCAACTCACTCTTCATGCTCATACCCTTCACAGTTTCCCTGGTAGCTTTT
TTCGTGCTCTTTCTCTCACTGTGGAAGCATCACAAGAAGATGCAGGTCAATGCCAAAGGA
CCCAGAGATGCCAGCACCATGGCCACACAAAAGCCTTGCAAATTGGGTTCTCCTTCCTC
CTGCTGTATGCAATATACTTACTTTTCATTATCACAGGAATTTTGAACCTTGACTTGATG

AGATGTATAGTAATACTTTTATTTGACCACATATCTGGAGCAGTTTTTCTATAAGCCAC
 TCATTTGTGCTGATTCTGGGAAACAGTAAGCTGAGACAAGCCACTCTTCTGTGCTGCCT
 TGTCTTAGGTGCCGGTCCAAAGATATGGACACTGTCGTTTTCTAAATAAATCCAGAGTAC
 ATTATGCAAAATCTTGAGGGTGATCAGTTCATAGAAAAAGTAATCTTAGAGGGGAAAATA
 5 AAATATTGGGGCTTCAAATGTTGGATGGGTAATACATAGGAAGGCAGGACAAGGATGAAG
 GAGACTAGCATTATATAAGTGATTTACAGGGGAAATGGGAAAGAGGGCTTTTATATAAT
 GAAGAAGAAGATAAATGATGAAGGATGAGGAAGAGTTAAATATGTAAAATGACAATAGAG
 ATGGCATCATGCCGTTTTAAGAAATTTGGAATGCATATGTATGTTTATATATTTTTTAAT
 TTTTATTGAATATATTTATTTACATTTTAAATGTTATCCTGTTTCCCCACCCAACCTCC
 10 CACCTCTTCCCACCTCCTTGCCCTGACATTCCCCTGCACTGGGGAATCCAGCCTTGACAG
 GACCAAGGGCTTCTCCTCCCTTTGTTGCCAACAAGGCCATTCTTTGCTACATGTGCAGCA
 GGAGCCATGGATCTGTCTATGTGTACTCTTTGGATGGTGGTTTAGTCCCTGGGAGCTCTT
 GTTGGTTGGTATTGTTGTTCTTATGGTGTGCAACTCCCTTCAGCTCCTTCAATCCTTCC
 TGTAACTCCTCCAATGTGGACCCTGTTCTCAGTCCAATGGTTGACTATGAGCATTACCT
 15 CTGTGATTGTCATGCTCTGGCACAGCTTCTCAGAAGACAGCTACATCAGTCTCCTATAAG
 AGTGCACCTTCATGGCATCAGCAATGTTGTCTTGATTTGGTGTCTGTATGTATATGGGCTG
 GATCCCAGGTGGGGCAGGCGCTGAATGGTCATTCCCTTCAGTCTTTGCTCCAACTTTGTC
 TTTATATCTCCTATGAATATTTTTGTTCCCCCTTATAAGAATGACTGAAGTATCCACACT
 TTGGCCATCCTTCTTCATGAGCTTCATGTGGTCTGTGAATTGTACATTGTGTAATCCAAG
 20 CTTTTGGGCTAATATCCAATTATAGTGAGTGCATACCAAAAAAAAAAAAAAAAAAAAAA
 AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

SEQ ID NO:81

25 Rat T2R03 amino acid sequence

MVPTQVTIFSIIMYVLESLVIIVQSCTTVAVLFREWMHFQRLSPVEIILISLGISHFCLQ
 WTSMLYNFGTYSRPVLLFWKVSVVWEFMNVLTFWLTSLLAVLYCVKVSSFHPVFLWLRL
 KILKLVLWLLLGLIASCLSIIPSVVKYHIQMELLTLDHLPKNSSLILRLQMF EWYFSNP
 30 FKMIGFGVPFLVFLISIIILLTVSLVQHWGQMKHYSSSSSLRAQCTVLKSLATFFIFFTS
 YFLTIVVSFIGTVFDKKSFWVCEAVIYGLVCIHFTSLMMSNPTLKKALRLQFWSPESS

SEQ ID NO:82

Rat T2R03 nucleotide sequence

GCATGGTGCCAACCCAAGTCACCATCTTCTCTATCATCATGTATGTGCTTGAGTCCTTAG
 TCATAATTGTGCAAAGTTGCACAACGGTTGCAGTGCTGTTTCAGAGAGTGGATGCACCTTC
 5 AAAGACTGTCGCCGGTGGAAATAATTCTCATCAGCCTGGGCATTTTCACATTTCTGTCTAC
 AGTGGACATCGATGCTGTACAACCTTTGGTACCTACTCTAGGCCTGTCCTTTTATTTTGGGA
 AGGTATCGGTCTGCTGGGAGTTCATGAACGTTTTGACATTCTGGCTAACCAGTTTGCTTG
 CTGTCCTCTACTGTGTCAAGGTCTCTTCCTTCTCTCACCCCGTCTTCCTCTGGCTGAGGT
 TGAAAATTTTGAACTGGTTCTCTGGTTGCTATTGGGCGCTCTGATAGCTTCTTGTTTGT
 10 CAATCATCCCTTCTGTTGTTAAATATCATATCCAGATGGAATTACTCACCTAGATCATT
 TACCCAAAACAGTTCTTTGATTCTAAGACTGCAAATGTTTCGAGTGGTATTTTCTAATC
 CTTTCAAATGATTGGGTTTGGCGTTCCTTTCCTCGTGTTCTGATTCTATCATCTTAC
 TCACAGTCTCGCTGGTCCAGCATTGGGGGCAGATGAAACACTACAGCAGCAGCAGCTCCA
 GCCTGAGAGCTCAGTGCCTGTTCTGAAGTCTCTTGCCACCTTCTTCATCTTCTTCACAT
 15 CCTATTTTCTGACTATAGTCGTCTCCTTTATTGGCACCGTGTTTGATAAGAAGTCATGGT
 TCTGGGTCTGCGAAGCTGTCATCTATGGTTTAGTCTGTATTCACTTCACTTCCCTGATGA
 TGAGCAACCCTACACTGAAAAAGCACTCAGGTTGCAGTTCTGGAGCCAGAGTCTTCCT
 AAGGCAGGGAATTCAGTGAAGCCTCTGGGGTAAGGAGGCTTTGCATTGGCACAGTTCTTA
 GAGTGAAATGCAAACGTGGACACGAACCTTCATTCTCTTTCATGTCCACAGATGGATGGAT
 20 CTATAAATCATCACCAATCTTCCCTGTATTCTGACCCATCCTTTTCCTGTCCTATCCATA
 GTCCCCAGGTTGGTTTTGATTTTTCTCATGATCACACCTTAGCTTTAGCCACCGTTGCAA
 TATCAAACATGATCTATATGTTACAGCCAAAATCATTCTCACAATTGTCAATTGCTTCAC
 AAATTCAGATAAATCCCCCTTCCTGTCAGGAATGTATTGTCTGTGCATTCAATGCTCACC
 ATGCTAAGCCATTCAATCCCTTCCTAACTTGAGTTTAAGAAGAAAATGTCTTACTGTTGC
 25 CCATGTCCTATTGTGCTGCTTCTGGATGTTTTATGCAGTGATTTAGACACACGCCCTTGC
 CTGTCTCCAAATACTGGCCCTTTATTCCTTTATAAGTCTAGTAGAAAATGAACTCGTCTT
 TACTTCATTGACGAAGACATTGTATTCTTCCCCAAAATAGTGTTTAACTACTCTAGTCTC
 ATCCATAATATCCCTAAATATCAGTGATTTAGTGAGTAAACCTGACAACAGTTATTGC
 TTTGACTCTTAATTCAATTGTGCTGTAACATAGAGGAAACATTCTAGAACATTTCCATAT
 30 TAATTTGTGCTTGTAGCAAACCAAAATTCTCCCCAGTTGGGTAAAAATATCAAAAGCACA
 GAGTAATCAATTTTGAAATCACTCAGAAGACATCATTGTTCTATATATGTTTTTTTTAAA
 CTTCCCTCTAACAAGTATCAGATCTTTGCCTTTACAGGGTCTGGTCTTACCATGACTATA
 TTTTATCACCATGACCTATTTTCTCTTCATCTCTTTGTTTTCACTAACTCAGTAGCAACC
 AAATATCACATTAATAGCTAACTCTGGGCACTTATTTCTCAGCCTTTATCTATTCCAGAC

TTTACAAGGGAAAGTGACTCTTCAGATTTAAGTTTAAAATTAGAAGAGAGATAAATTTCA
CAAGCTTTCACTCCTAAGGCTAAAGATAGGCTGTGTAGGTAGTTATTTCTGAGCACATTG
GCACATCACCATTGTCAGTACTTGAGGGTTTGAATGAAGCTCAAGAAGCTTGGAAA
GAAGGTGGTCTTCTGACATCAATCAAGAAACAAGCTTTCCTCCCTACTTCTTCCCTAAAT
5 GCAACAACCTAAGAATTATCCACAAGATGGATGGCGCAAGGGTTCCTCAATCAATTTAG
GATGTACATCAATGCGCAGCCTATACTACACCGAAAAGGAAGCGCATGGGTCTTAAAAAG
TAAAGGGGATATCAAAAATTCGCAACCAACAAAAAGTGGCACACATTTAAGCTAGGTC
TATGTTTGGTCAGTTACACCTGGAGAAGGGGGACATTTGGTCAGCTCATTCGAACACTGT
CAAGTCCTACCAACAATTCCTCTATGCTATTACCCATTAAACCTCAGGTCTCATCGAAAA
10 AAAAAAAAAAAAA

SEQ ID NO:83

Rat T2R04 amino acid sequence

15 MLSAAEGILLCVVTSEAVLGVLGDTFIALANCMYAKNKKLSKIGFILIGLAISRIGVW
IIILQGYMQVFFPHILTFGNITEYITYIWVFLNHLVWFATNLNILYFLKIANFSNSVFL
WLKSRVRVVFIFLSGCLLTSWLLCFPQFSKMLNNSKMYWGNTSWLQQQKNVFLINQSLTN
LGIFFFIIVSLITCFLLVFLWRHIRQMHS DGSLRDLNTEAHVKAMRVLISFAVLFILH
20 FVGLSIQVLCFFLPQNNLLFITGLIATCLYPCGHSIILILGNKQLKQASLKALQHLTCCE
TKRNLSVT

SEQ ID NO:84

25 Rat T2R04 nucleotide sequence

TGGTTCATCACATGACAATAGGCTTGAAAACTTGCAGATAGAGAAGACATAACCCCTC
CAACAAGAAGCCAACATATGGGACATTCTCCAGCAGATAATTTATAACAGATGCAACGGG
AGCAACTTCGAGATCTGCAAAG**ATGCTGAGTGCGAGCAGAAGGCATCCTCCTTTGTGTTGT**
30 **CACTAGTGAGGCAGTGCTGGGGGTTTTAGGAGACACATTCATTGCACTTGCAAAGTGCAT**
GGAGTATGCCAAGAACAAGAAGCTCTCTAAGATTGGTTTCATTCTCATTTGGCTTGGCGAT
TTCCAGAATTGGTGTCGTATGGATAATAATTTTACAGGGGTATATGCAAGTATTTTTTCC
ACACATACTTACCTTTGGAAACATAACTGAATATATTACTTACATATGGGTGTTTCTCAA
TCACCTAAGTGTCTGGTTTGCTACCAACCTCAATATCCTCTACTTTCTAAAGATAGCAAA

TTTCAGGGATTTTTGTGTTTCCTCTTTAAGGGCTTCTACTTGTTTACTTGTGTTGTCCTG
TATTTCTTTAAGGTAGTTATTTATGTCCTTCTTGAAGTCCTCCATCATTATCAAAAAATG
TGATTTTTTAAATATAAACCTTGCTTTTCTGGTGTGTTTGGATGTCAAGTATTTTCTTTGC
TGGGAGAACTGGGCTCTGATAATGCCAAGTTGTTTGATTTCTGTTGCTTAGTTTCCTGTT
5 CTTGCCTCTCGCCATTGGGTTTTCTCTGGTGTGTTGCTTATCTTGCTGTTTCTGAGAGTGG
CTTGACACTCTTGTAGGCATCTGTGTCAGGCCTCCTGTAGAACTGTTTCCCTGTTTTCTT
TCAGCCTTTTCTGAGAACAGGTGCTCTGATCTCAGGTGTGTAGGCATTCCTGGTGACTAT
CTTTCAGCTTTAGGAGCAGGCAGGAATCAGAAGGGTCCTGTCCCTGACTGCTCCTAGATC
CTTGCACCCAGGGGGCACAGTTAGCACTAGGCAATTCCTCTTGTTGTAGGGAATGTGGGT
10 AGAGGATAGTCGCCTCTGATTTCTCAGGAATGTCTGCACTTCTGAAAGTCCAGCCCTCTC
CCCCACAGGATTTAGGTGCAGGGAGCTGTTTGACCACTTCAATTCAGTCCTGGGTGTAGA
CCAGAACCACAGGTAAAAAGAATGACTTCATTAAATTAGCAGACAAATGGGTGGAACATA
GAAAATGTCATCCTGGGCTGGAGAGATGGCTCAGTGTTTCCAGACCACTGGCTGCTCTTCC
AGAGGTCCTGAGTTCAATTCCTCAACAATACTATATGGTGGCTACCAACCATTACAATGAGAT
15 CAGATGCCCTCCTCTTGTGTATCTGAAGAGAGTGACAGTGTAATTACATACATAAAATAA
ATAAATAAATCTAAAAAATGTTAAAAA

SEQ ID NO:85

20 Rat T2R05 amino acid sequence

MLGAMEGVLLSVATSEALLGIVGNTFIALVNCMDCTRKNLYNIGFILTGLAISRICLVW
ILITEAYIKIFSPQLLSPINIIEILISYLWIITSQLNVWFATSLSIFYFLKIANFSSHIFL
WLKRRINIVFAFLIGCLLSWLFSPVVKMVKDKKMLYINSSWQIHMKKSELIINYVFT
25 NGGVFLLFIIMLIVCFLLIISLWRHSKWMQSNESGFRDLNTEVHVKTIKVLLSFIILFIL
HLIGITINVICLLVPENLLFVFGLTIAFLYPCCHSLILILANSRLKRCFVRILQQLMCS
EEGKEFRNT

30 **SEQ ID NO:86**

Rat T2R05 nucleotide sequence

AAGAGATTTTCAGATACTACCACAAACATTTTTTAAATATATGTAAGTCTTTAAAGAAAGA
AGGGAAAGCCACTCCTTTATTGAGCAGCCAATAGATTGCCATCTTAAATTCTGTGGCAG

AAGCTATTTTAAAGATCTGCGAAGATGCTGGGTGCAATGGAAGGTGTCCTCCTTTTCAGTT
 GCAACTAGTGAGGCTTTGCTTGGCATTGTAGGGAACACATTCATTGCACTTGTGAACTGC
 ATGGACTGTACCAGGAACAAGAATCTCTATAATATTGGCTTCATTCTCACTGGCTTGGCA
 ATTTCCAGAATCTGCCTCGTGTGGATCTTAATCACAGAGGCATACATAAAAATATTCTCT
 5 CCACAGTTGCTGTCTCCTATCAACATAATTGAACTCATCAGTTATCTATGGATAATTACC
 AGTCAATTGAATGTTTGGTTTGTACCAGCCTCAGTATCTTTTATTTCTCAAGATAGCA
 AATTTTTCCCACCACATATTTCTCTGGTTAAAAAGAAGAATTAATATAGTTTTTGCCTTC
 CTGATAGGGTGCTTACTTATGTCATGGCTATTTTCTTTCCAGTAGTTGTGAAGATGGTT
 AAAGATAAAAAAATGCTGTATATAAACTCATCTTGGCAAATCCACATGAAGAAAAGTGAG
 10 TTAATCATTAACATATGTTTTACCAATGGGGGAGTATTTTTACTTTTTATAATAATGTTA
 ATTGTATGTTTTCTCTTAATTATTTCCCTTTGGAGACACAGCAAGTGGATGCAATCAAAT
 GAATCAGGATTCAGAGATCTCAACACAGAAGTTCATGTGAAAACAATAAAAGTTTTTATTA
 TCTTTTATTATCCTTTTTATATTGCATTTAATTGGTATTACCATCAATGTCATTTGTCTG
 TTAGTCCCAGAAAATAACTTGTTATTCGTGTTTGGTTTGACGATTGCATTCCTCTATCCC
 15 TGCTGCCACTCACTTATCCTAATTCTAGCAAACAGCCGGCTGAAACGATGCTTTGTAAGG
 AACTGCAACAATTAATGTGCTCTGAGGAAGGAAAAGAATTCAGAAACACATGACAGTCT
 GGAAGACAAACAATCAGAAATAGTAAGTGAAAAAAAAAAAAAAAAAAAA

20 **SEQ ID NO:87**

Rat T2R06 amino acid sequence

EALVGILGNAFIALVNFMGWMKNRKITAIDLILSSLAMSRICLQCIILLDCIILVQYPDT
 YNRGKEMRIIDFFWTLTNHLSVWFATCLSIFYFFKIANFFHPLFLWIKWRIDKLILRTL
 25 ACLILSLCFSLPVTENLADDFRRCVKTKERINSTLRCKLNKAGYASVKVNLNLVMLFPFS
 VSLVSFLLLILSLWRHTRQMQLNVTGYNDPSTTAHVKATKAVISFLVLFIVYCLAFLIAT
 SSYFMPPESELAVIWGELIALIYPSSHFILILGNSKLKQASVRVLCRVKTMKGRKY

30 **SEQ ID NO:88**

Rat T2R06 nucleotide sequence

GTGAGGCCTTAGTAGGAATCTTAGGAAATGCATTCATTGCATTGGTAAACTTCATGGGCT
 GGATGAAGAATAGGAAGATCACTGCTATTGATTTAATCCTCTCAAGTCTGGCTATGTCCA

GGATTTGTCTACAGTGTATAATTCTATTAGATTGTATTATATTGGTGCAGTATCCAGACA
 CTTACAACAGGGGTAAAGAAATGAGGATCATTGATTTCTTCTGGACGCTTACCAACCATT
 TAAGTGTCTGGTTTGCCACCTGCCTCAGCATTTTCTATTTCTTCAAGATAGCAAACCTTCT
 TCCATCCTCTTTTCTCTGGATAAAGTGGAGAATTGACAAGCTAATTCTGAGGACTCTAC
 5 TGGCATGCTTGATTCTCTCCCTATGCTTTAGCCTCCCAGTCACTGAGAATTTGGCTGATG
 ATTTTCAGACGCTGTGTCAAGACAAAAGAAAGAATAAACTCTACTCTGAGGTGCAAATTAA
 ATAAAGCTGGATATGCTTCTGTCAAGGTAAATCTCAACTTGGTCATGCTGTTCCCCTTTT
 CTGTGTCCCTTGTCTCATTCTTCTCTTGATTCTCTCCCTATGGAGACACACCAGGCAGA
 TGCAACTCAATGTAACAGGGTACAATGATCCCAGCACAAACAGCTCATGTGAAAGCCACAA
 10 AAGCAGTAATTTCTTCTAGTTCTGTTTATTGTCTACTGCCTGGCCTTTCTTATAGCCA
 CTTCCAGCTACTTTATGCCAGAGAGTGAATTAGCTGTAATTTGGGGTGAGCTGATAGCTC
 TAATATATCCCTCAAGCCATTCATTTATCCTGATCCTTGGGAACAGTAAACTAAAACAGG
 CATCTGTAAGGGTGCTTTGTAGAGTAAAGACTATGTTAAAGGGAAGAAAATATTAGCATC
 ATGGATATATTTGAAGAAAACTATCACTGTCTAAAGAAAAAGGATGACAAATCATTATC
 15 TTTCAATTCTTATATGAATATTGCTTTCATGCGGTAAACATCTTTTAACAAACTTAAATCAA
 ATGTTGGGAAATCTCATATACAGCAACTTTGCATGTCTCTCTGTCTATTTCCCTCTCCCT
 TTGTACATAGTTGACATAAAAAAAGAATTTTCATGACAAAATTGTAATAAATAGCTACAG
 AGGCAGCACATTTTCATAGTAAGTTCTGAATCACTCTTCCAAATGCAAAGCTGCCTGACA
 AATTCAAAACAACTGTAACAGTATTTCACTGCTGTTTGCATTCTTTGGAAAAGCAGGTGG
 20 TTTGTTCCCTATGACCTGACTTGGAGTTTTCTTCTTACATCACTG

SEQ ID NO:89

Rat T2R07 amino acid sequence

25 MGSSLYDILTIVMIAEFIFGNVTNGFIVLTNCIAWLSKRTLSFIGWIQLFLAISRVVLIW
 EMLLAWLKYMKYSFSLAGTEL RVMMLTWVVS NHFSLWLATILSIFYLLKIASFSRPVFL
 YLKWRVKVLLLLILGNLIFLMFNILQINTHIEDWMDQYKR NITWDSRVNEFVGFSNLVL
 LEMIMFSVTPFTVALVSFILLIFSLWKHLQKMHLS SRGERDPSTKAHVNALRIMVSFLLL
 30 YATYFISFFISLIPMAHKKGLDLMFSLTVGLFYPSSH SFILILGHSNLRHSSCLVITYLR
 CKEKD

SEQ ID NO:90

Rat T2R07 nucleotide sequence

CAGTAGCAAAATTTTACTATGTTTCATTGATATTATGTCA_nGnCACTACGTAAGAAGGAAG
 ACTTGAAAGAAAGCTTATCTGAGTTTTTAAGAATACATGGACATTTTCAGCTTGGCAAATG
 5 ACGAGCTGTGAATTTTTGTCATCTGGAC**ATGGGAAGCAGCCTGTATGATATCTTA**ACTAT
TGTCATGATTGCAGAGTTTATATTCGGAAATGTGACCAATGGATTCATAGTGCTGACAAA
CTGTATTGCTTGGCTCAGTAAAGAACTCTTTCTTTCATTGGTTGGATCCAGCTTTTCTT
 GGCCATTTCCAGAGTGGTTTTTGATATGGGAAATGTTACTAGCATGGCTGAAATATATGAA
 GTATTCATTTTCATATTTGGCTGGCACAGAATTAAGGGTTATGATGTTGACCTGGGTTAGT
 10 **TTCCAATCACTTTAGTCTCTGGCTTGCCACCATTCTAAGCATCTTTT**ATTTGCTCAAAAT
 AGCTAGTTTCTCCAGACCTGTTTTCTGTATCTGAAGTGGAGAGTAAAAAAGTGCTCCT
 GCTGATTCTTCTCGGAAATTTAATCTTCCTGATGTTCAATATATTACAAATCAACACTCA
 CATAGAAGACTGGATGGATCAATATAAGAGAAATATAACGTGGGATTCCAGAGTGAATGA
 ATTTGTGGGGTTTTCAAATCTGGTTTTATTGGAGATGATTATGTTCTCTGTAACACCATT
 15 **CACCGTGGCTCTGGTCTCCTTCATCCTGTTAATCTTCTCTTT**ATGGAACATCTCCAGAA
 GATGCATCTCAGTTCAGAGGGGAACGAGACCCTAGCACAAAAGCCCATGTGAATGCCCT
 GAGAATTATGGTCTCCTTCCTCTTACTCTATGCCACTTACTTCATATCCTTTTTTTATATC
 ATTAATTCCTATGGCACATAAAAAAGGACTAGATCTTATGTTTAGCCTAACTGTTGGACT
TTTCTACCCTTCAAGCCACTCATTTATCTTGATTTTGGGACATTCTAATCTAAGGCATTC
 20 **CAGTTGTCTGGTGATAACCTATCTGAGATGTAAGGAAAAGGATTAG**AAATTCACTATTCC
 ATAAGGCAGTTAAACCACATGCTATTAGGTATACTCAGTGCTAGATCCCTAGGCAAGCAT
 TAACATTAAAAATATATAATTTCTAGATTCTTCTATTTGTGATAAACCACTCACTTAGAA
 TAATGCTAAAGTAGCGTGATGTTGTATATAAGTGTAAGAATAAAATGTAATTAATTTAGT
 TTAGGCACAATAACATATGTCTACTAAGTAAAACTAGGCAGGCTGCTACACGCATATTA
 25 GAATCCAGGCTGAGGTATATAGACTCAAGAAATACTGTGGAATAAAGATTTTAATTTTCA
 TTCTATTGTGAGTTATGTGAAATCAATGCCATTAAAGGCATACACAAGATTTTCACACAC
 TGAAACAACCTTCTTGCATTTTGTTCATATTGTATTGGAAGTAAATTGGAGATAAACTTAAT
 ATCAATAAATTACAAAATGTAAACATAAACAGGGTGATTAAAAATTAGCCTCTAGGTCCT
 GGGGAAATGATTCaAGTAAAGTGCTTTCTTTCAAATAGGAGAATCTGATTGTAAATCAT
 30 CTAAAAGTCTGGCATAAAATGTCAATGAAAATTGTATGTAAATATAGCTATgGCmAAGA
 GCACCmAAGAAAAGAAAATTTTTGCCTTTGAAACCCAGTAATTGATATCCTTTAAAAAAG
 CAGTTACATATTTTTCTGTTTAAGATTTTGTCAAAGGGTAGCTTTGACAACATAATATAAG
 CTGAGGAAGGTAGCAAGTGTGAAGTCAGCTAATGGGGTCAGTCAAGTGCTGTTAGCAGCA
 GATGGAGGCCACTGCTGAATTTAGCAGGCAATTTACAGGGTGAGCACTGCTAGTGCTGAC

AGAAGAAAACTCTGAAATTTTAACTCTTTAGGGTCTGGTGAGAAAGAAAAAGAGAGAAA
 ATCGCATA
 TCATGGAAGCTCTAACAAGTTGACTCAAACAACCTTTATGATGTTTTTAGGCCCTTTTATT
 TTAATGTCAGTGAATTAGGTGTGGTACAGCAATATTGCTACTTTTAAATTCAAAGCAGT
 5 GTTTTATATATTATTCATTATATAAGCTAATTATAAGTTTAAATCAAAAGGTTTATTTGT
 CCATGATTTTACTTTATCATTGGGCACACCTGTGCTCTCATCCTTGGGCTTGACCTAGAA
 TGAAAGTTTATCCTTGATCATATGTCTGTCAAGACTACTTCTCTCCTATAGTAGTTT
 ATGTACTTACAATATACAAAAGTTTATTGAATTCCTTTTATCACTTATGCAGCCTTTTCT
 TACTATTCTATTCTATTCTATTCTATTCTATTCTATTCTATTCTATTCTATTCTATTCTA
 10 TTCTATTCTATTCTATTCTAGAACTAACCTATACATTCATTTCTGGCAAAACAACCTTAT
 ATCATCTCCTTAATTATTTTATCAATTAATCTAACATCCTGAAGTTATTTAAATCTAATA
 TAAGGACTCTGTAAAGTCACAAATTTATTTATACTTCACAAAATTCATTATTTTATGGAA
 CTGCAGCATTGCCTGGGCCAGGAGTCACAAGAGTTCCAGAGTTGACTTTATTGGCATCTG
 CCTGGCTAACTGAAGGATCAGTTTTCTGTGTACAATAATTTTGTGTATCTCTTTTGATGC
 15 AAGATATGAAAAATAATTTAGTCTAAAAGTGTCTTAAATTTGAAACTCTCTGGCCAGA
 ATCTAACTATTGATGACCAGTTTGCACCATGGACTCAGTGTCTTCTATTGCTTTAAAATA
 AGCAACATCTTGAATGCTTTTCTTGTGTATTAGGCAAATAATTAACAACATGTTTCTATG
 ATTGTCTCAATAACAATACTATATTTCTCACAGTTTTTAATTTTTATGGCAAAGTTGGCT
 AATAAGAATTTTTTTCAAATTATCAAACGTGAAGAAAACCTTGACATTTTATTCATGGAG
 20 ATTCTAAATGTTTTCTTAGCATATTGCCTTTTTTACTAAGTTGATTTTTATCATGTTTTGG
 TAGTATTTCTAATTTTCTTTTTTCTAAGTATGTTATGTAGTAACACCAGGAGAAATGAA
 ACAAATGACATTTATACTAAGGATGTGACAAATAAGGCCCAAAGAAAGTTTTGAAAATCA
 TGATCTCATTTCTATTCTTCTTTATTAAGTATAGCATAAGCAAATCTGATGGTGGTCT
 TGGCCCATATCTTTGAACACAGTGTAGTGGTGAAGACTTTTTCAAATATTATGTCATATT
 25 TGTACCCATCTCTGTACCTATTTCTTCTGATTTTCATGAGGAAAAAATGAGGAAGGGTTTG
 TTTGTGTGCTGGAGCAGCTGAAGTGGACCAAGGGGCAGGAATTCTCTCTGTTCCGGTCCTA
 GTGTGACTGATGATGCTCTCATTGAAAAACAGGAAGAAGAAGAAAGACTTTATATGCACC
 ATTCACTCCTTCCCCCTCCTACATTCCACCTCCCTCTTGAAAGAGTGTCTATCTATATAG
 ATATAGCTATCCTGAAATCCATTAAGTAGACCTGACTGGCTTAAATCTCACAGAAATTCA
 30 CCTACCTTTTCCATGATTGCTGAAATTAAAGACATGTGCCGACATATTGGGCACATTGAG
 ACCTTTTGCCAACTGTCTTTCAACTCATTTGGACCTACTGAGAAGTATTCAAATATTTG
 GTTGTTTTAAATAAAAGGAAAGTGGGTCTATATTACTTGAATTGGATAGAGAAATTTTCA
 CTTACAAGTGATATTGAAAATGGGGGAGAATGTATTTTAGCATAAGCACCAGAACACAAA

GCAATTCTTGTTAAACTTTATCGATAAATTGGATAAATGTTAAAAAGAAAAATAAAA
TATACGAAC TATTATGAAAAAAAAAAAAAAAAA

5 **SEQ ID NO:91**

Rat T2R08 amino acid sequence

MEPVIHVFATLLIHVEFIFGNLSNGLIVLSNFDWVVKRLSTIDKILLTLAISRITLIW
EMYACFKIVYGSSSFIFGMKLQILYFAWILSSHFSLWFATALSIFYLLRIANCSWKIFLY
10 LKWRLKQVIVGMLLASLVFLPGILMQRTLEERPYYGGNTSEDSMETDFAKFTELILFNM
TIFSVIPFSLALISFLLLI FSLWKHLQKMQ LSSRGH GDPSTKAHRNALRIMVSFLLLYTS
YFLSLLISWIAQKHHSKLVDIIGIITELMYPVHSFILILGNSKCLKQTS LWILSHLKCRL
KGENILTPSGKPIN

15

SEQ ID NO:92

Rat T2R08 nucleotide sequence

CTGCAGGTTGGTGATCCAGTAATGAGCAGCACTGTTATATCTCAGGCTTTCTAAGATCAT
20 **GGAACCTGTCATTCACGTCTTTGCCACTCTACTAATACATGTGGAGTTCATTTTTGGGAA**
TCTGAGCAATGGATTAATAGTGTGTCAAACCTCTGGGACTGGGTCGTTAAACGAAAAC
TTCCACAATTGATAAAATCTTCTTACATTGGCAATTTCAAGAATCACTCTCATCTGGGA
AATGTATGCTTGTTTTAAATTTGTATATGGTTCATCTTCATTTATATTTGGGATGAAGTT
ACAAATCTTTATTTTGCCTGGATCCTTTCTAGTCACTTCAGCCTCTGGTTTGCCACAGC
25 **TCTCAGCATCTTTTACTTACTCAGAATAGCTAACTGCTCCTGGAAGATCTTCCTGTATCT**
GAAATGGAGACTTAAACAAGTGATTGTGGGGATGTTGCTGGCAAGCTTGGTGTTCTTGCC
TGGAATCCTGATGCAAAGGACTCTTGAAGAGAGGCCCTATCAATATGGAGGAAACACAAG
TGAGGATTCCATGGAAACTGACTTTGCAAAGTTTACAGAGCTGATTCTTTTCAACATGAC
TATATTCTCTGTAATACCATTTTCATTGGCCTTGATTCTTTTCTCCTGCTAATCTTCTC
30 **TTTGTGGAAACATCTCCAGAAGATGCAGCTCAGTTCAGAGGACATGGAGACCCTAGCAC**
CAAGGCCACAGAAATGCTTTGAGAATTATGGTCTCCTTCCTCTTGCTCTACACTTCATA
TTTCCTGTCTCTTCTTATATCATGGATTGCTCAGAAGCATCACAGTAACTGGTTGACAT
TATTGGTATTATTACTGAACTCATGTATCCTTCAGTCCACTCATTTATCCTGATTCTAGG
AAATTCTAAATTAAAGCAGACTTCTCTTTGGATACTGAGTCATTTGAAATGTAGACTGAA

AGGAGAGAATATTTTAACTCCATCTGGCAAACCAATTA**ACTAG**CTGTTATATATTCTGTA
 TTGCAAACAAATCAGTGAGTTAGTGGTTCAAGGATTCCATCCTTGACTTATTGTATCATG
 GAAGTCATATAGGGAGAGGCTGAACAAGCTATCTTCTGTAAATTGGCAAGGGTGCATAT
 AGTACTGGTACTGGGACACCATCCAACCATAAAACCTTCTAACCATAACCTACCTGACTG
 5 CAAGATATGCTGGGACAATGGTGGCTCAGAGATTTTGGGACTGGCCAACCAATGTCTATT
 CTTTCTTGAGGCTCACTCAATAAGGAGGCCATGCCCAACTCGTCcTGGATGGCCAGGAAC
 CAGAATCTCTGATGGsCCAATGATCTATGGnAGAACCCAGCATTACTGGGAAAAAAGAAT
 AATCACTTTGATGAATGGTCAAATATTTCCCTAAATATATTCTGATACACTTGTACATCAT
 TTCTCTTTCCCAATCATCATCACAGGGACTTCTCCCCAGCACCTGATGGGAACAGATACC
 10 AAAATCTACAGCCAAATACTAAATGCAGGTTGGGGAACCTCCACAAAAGACTGGAAGGAAG
 TACTGTGAGAGCCAGAGTGGTCCAGAACACTAGGAGAACACAGAACATCGAATTAACATA
 GCAGCACTCATAGGGTTAATGTAAAATAAAGCAGCAGTCACATAGACTGCACAGGTGTAC
 TCTAGATCCTCTGCATATATGTTGTGGTTGTCAAACCTTGGGAGTTTGTGGACTAATAA
 CAATGTGAATAAGTAAGTCTCTGACACTTATTCCCGCTCTTGGAACCCTTTTCCACATTT
 15 TGTATTGTCTTACCACCTTGATATGAAGGTTTCTGAATAGTCCAAAAAAAAAAAAAAAAA
 AAAAAAAAAAAAAAAAAAAAAAAAAA

SEQ ID NO:93

20 Rat T2R09 amino acid sequence

MLSAAEGILLSIATVEAGLGVLGNTFIALVNCMDWAKNKKLSKIGFLLFGLATSRI FIVW
 ILILDAYAKLFFPGKYLSKSLTEIISCIWMTVNHMTVWFATSLSIFYFLKIANFSHYIFL
 WLKRRTDKVFALLWCLLISWAISFSFTVKVMKSNPKNHGNRTSGTHWEKREFTSNYVLI
 25 NIGVISLLIMTLTACFLLIISLWKHSRQM QSNVSGFRDLNTEAHVKAIKFLISFIILFIL
 YFIGVAVEIICMFI PENKLLFIFGLTTASVYPCCHSVILILTNSQLKQAFVKVLEGLKFS
 ENGKDLRAT

30 **SEQ ID NO:94**

Rat T2R09 nucleotide sequence

GGACACTGCAGCAGATCTGCTATAGAATAACAGATACAAACATAGCAACCTGCAGAG**ATG**
CTCAGTGCAGCAGAAGGCATCCTTCTTTCCATTGCAACTGTTGAAGCTGGGCTGGGAGTT

AAATAGTGGACAATTCAGTCCAGGACCTGAATGAGGTAGACAATGTCCTGTTAAGGGTTG
 GAACAAATATATAGATATGGTCATTCATATACAGAAACCTACAGGCGTGTTTGAACCTCTT
 GGTCTCTCAGTAATCAATTCTTAAATCTTTTTTAGAATGGATTTTTTATCATCATTCATG
 ATCTCTCAGCAGAGTCTGCAGGGGCTAAGAGACACACTAAGAGTATCTGGAGGGGGGAGT
 5 GTCTTCCTGCTCTATCAACCCCTAAAGTCATATATAACAATACAAAATTCACATTAGTT
 AAGTTCTTTTTTTTACATCTTTATTAAATTGGGTATTTCTTATTTACATTTCAAATGTGA
 TTCCCTTTCCTGGTTTCCAGGCCAATATCCCCCTAACCTCTCCCCTTCTATGTGGGTATT
 CCCTCGTGCCGAATTC

10

SEQ ID NO:95

Rat T2R10 amino acid sequence

MFLHTIKQRDIFTLIIFFVEITMGILGNGFIALVNIVDWIKRRRISSVDKILTTLALTR
 15 LIYAWSMLIFILLFILGPHLIMRSEILTSMGVIWVNNHFSIWLATCLGVFYFLKIANFS
 NSLFLYLKWRVKKVVL

SEQ ID NO:96

20 Rat T2R10 nucleotide sequence

CCCGGGCTGCAGGATTCGGCACGAGAATGAAACTTTTGCTCTACTATTTTGCTGTTCTG
 TGATACCACAGACCATAAAACAATCGAGCCAAGGGATCAAGAGCTGAACTTCAGAAAGT
 GGAATCAAATTTCTTCCTGATAGGTTAGCTTATGAGAATTCAGCATCTTATTCAACTT
 25 CAGAAAATTGGATATAAGATACAGTGTCTGGATGAAGCCGAATTGATCTATTTGGGGAGA
 AAAACGCCAACATTTATAATAAGGTTTTATGAGACAGTTCCTGGGAAATTTGGATATTT
 CCTAGTTAGTAATGTGTAAATGGGATTTTAAAACATGATTATTTTGTATTTTAAACAACC
 AACATGAGGAGCTTTTTAAATGCCACTTAGACATTATAAACTGAAGC**ATGTTCTTACACA**
CAATAAAGCAACGTGATATTTTTACTTTGATAATCATATTTTTTGTGGAAATAACAATGG
 30 **GAATCTTAGGAAATGGATTCATAGCACTAGTGAACATTGTGGACTGGATCAAGAGAAGAA**
GGATTTCTTCAGTGGATAAGATTCTCACTACCTTGGCCCTTACCAGACTCATTTATGCGT
GGTCTATGCTCATTTTTATATTGTTATTCATACTGGGCCCGCATTTGATTATGAGATCAG
AAATACTTACATCAATGGGTGTTATCTGGGTGGTGAACAATCACTTCAGCATCTGGCTTG

CTACATGCCTCGGTGTCTTTTATTTTCTCAAGATAGCCAATTTTCTAACTCTTTGTTTC
TTTACCTAAAGTGGAGAGTTAAAAAGTGGTTTTAATG

5 **SEQ ID NO:97**

Rat T2R11 amino acid sequence

GSGNGFIVSVNGSHWFKSKKISLSDFIITSLALFRIFLLWIIFTDSLIIIVFSYHAHDSGI
RMQLIDVFWTFTHFSIWLIISCLSVFYCLKIATFSHPSFL*LKSR

10

SEQ ID NO:98

Rat T2R11 nucleotide sequence

15 GGATCCGGAACGGTTTTATCGTGTCAGTCAATGGCAGCCATTGGTTCAAGAGCAAGAAG
ATTTCTTTGTCTGACTTCATCATTACCAGCTTGGCCCTCTTCAGGATCTTTCTGCTGTGG
ATCATCTTTACTGATAGCCTCATAATAGTGTTCTCTTACCACGCCCACGACTCAGGGATA
AGGATGCAACTTATTGATGTTTTCTGGACATTTACAACCCACTTCAGTATTTGGCTTATC
TCCTGTCTCAGTGTTTTCTACTGCCTGAAAATAGCCACTTTCTCCCACCCCTCATTCCTG
20 TAGCTCAAATCTAGA

SEQ ID NO:99

Rat T2R12 amino acid sequence

25

MLSTVSVFFMSIFVLLCFLGILANGFIVLMLSREWLWRGRLLPSDMILLSLGTSRFCQQC
VGLVNSFYYSLHLVEYSRSLARQLISLHMDFLNSATFWFGTWLSVLFCKIANFSPAFI
WLKWRFPALVPWLLLSILVSFIVTLMFFWGNHTVYQAFRRKFSGNTTFKEWNRRLRID
YFMPCLKVTTISIPCSLFLVSILLINSLRRHSQRMQHNAHSLQDPNTQAHSRALKSLISF
30 LVLIALSYVSMVIDATVVISSDNVWYWPWQIILYLCMSVHPFILITNNLKFRGTFRQLLL
LARGFWVT

SEQ ID NO:100

Rat T2R12 nucleotide sequence

GTGTGAGGGACTGTGGGTAGGGGCTGGGAGGAGGCCAGGAACCAAGGCAACCAGTGGTGA
CAGGAGGGGCTGAAA**ATGCTATCAACTGTATCAGTTTTCTTCATGTCGATCTTTGTTCTGC**
5 **TCTGTTTCCTGGGAATCCTGGCAAACGGCTTCATTGTGCTGATGCTGAGCAGGGAATGGC**
TATGGCGCGGTAGGCTGCTCCCCTCAGACATGATCCTCCTCAGTTTGGGCACCTCCCGAT
TCTGCCAGCAGTGCCTTGGGCTGGTGAACAGTTTCTACTATTCCCTCCACCTTGTTGAGT
ACTCCAGGAGCCTTGCCCGTCAACTCATTAGTCTTCACATGGACTTCTTGAACTCAGCCA
CTTTCTGGTTTGGCACCTGGCTCAGCGTCCTGTTCTGTATCAAGATTGCTAACTTCTCCC
10 **ATCCTGCCTTCCTGTGGTTGAAGTGGAGATTCCCAGCATTGGTGCCTTGGCTCCTACTGG**
GCTCTATCTTGGTGTCTTCATCGTAACCTCTGATGTTCTTTTGGGGAAACCACACTGTCT
ATCAGGCATTCTTAAGGAGAAAGTTTTCTGGGAACACAACCTTTAAGGAGTGGAACAGAA
GGCTGGAAATAGACTATTTTCATGCCTCTGAAACTTGTCACCACGTCAATTCTTGCTCTC
TTTTTCTAGTCTCAATTTTGCTGTTGATCAATTCTCTCAGAAGGCATTCACAAAGAATGC
15 **AGCACAATGCTCACAGCTTGCAAGACCCCAACACCCAGGCTCACAGCAGAGCCCTGAAGT**
CACTCATCTCATTTCTGGTTCTTTACGCGCTGTCCCTATGTGTCCATGGTCATTGACGCTA
CAGTTGTCATCTCCTCAGATAACGTGTGGTATTGGCCCTGGCAAATTATACTTTACTTGT
GCATGTCCGTACATCCATTTATCCTTATCACTAATAATCTCAAGTTCCGAGGCACCTTCA
GGCAGCTACTCCTGTTGGCCAGGGGATTCTGGGTGACCTAGAAGGTTTGGTCTCTTTATC
20 **TGTACCCTTTGAAGAGACTTAGGTGAGGGTGACTTCCCTTGGAAGTGATCTCATCTACAT**
GGAAATGTCTTTGTAGGCTGACATGGGGTCATACTATGTGGTTCCTCCTTGGGAAAGAGG
AGAAGAAAATACAGGGATTCTGAGCGTTCTTCCTTATCTTGGGATATTATGAAAATGGAC
ATTCTGAATCCTGAACCAGTATTGATCTGAAGTGCAAAGTACAATATGCCTGTTCCCTTC
ATGTCTGCTATCCTCTTGGTACTTATTAATTCCCT
25

SEQ ID NO:101

Rat T2R13 amino acid sequence

30 MCGFPLSIQLLTGLVQMYVILIIAVFTPGLGNVFIGLVNYSWVKNKKITFINFILICL
AASRISSVLVVFIDAIILELTPHVVHSYSRVKCSDFWVITDQLSTWLATCLSIFYLLKI
AHFSLPLFLWLKWRLRGVLVGFLLFSLSLIVYFLLLELLSIWGDYVIPKSNLTLYSET
IKTLAFQKIIVFDMLYLVPFLVSLASLLLLFLSLVKHSQNLDRISTTSEDSRAKIHKKAM

KMLLSFLVLFIIHIFCMQLSRWLFPLFPNNRSTNFLLLTLNIFPLSHTFIIILGNSKLRQ
RAMRVLQHLKSQLQELILSLHRLSRVFTMEIA

5 **SEQ ID NO:102**

Rat T2R13 nucleotide sequence

GGGATTCAGTTGGATAAGAGAAAAGTCAAAACCCTAAGACTAAGAATTCCTTAAGTAGA
TATCAATTTCTATCCATTGGAAGGAGTTTCCAATCACACTGAAATTACAATAAAAAAGGA
10 GCAAGATAACTATGGGAAAGGATGATTTTCGGTGGATGTTTGAGAACTGAGCAGCAAGGC
AAATTGATAGATGTGTGGATTCCCTCTTTCTATTCAACTGCTTACTGGATTGGTTCAAAT
GTACGTGATATTGATAATAGCAGTGTTCACCTGGAATGCTGGGGAATGTGTTCATTGG
ACTGGTAAACTACTCTGACTGGGTAAAAACAAGAAAATCACCTTCATCAACTTCATCCT
GATCTGTTTGGCAGCGTCCAGAATCAGCTCTGTGTTGGTGGTATTTATTGATGCAATCAT
15 CCTAGAACTAACTCCTCATGTCTATCATTCTTACAGTCGAGTGAAATGCTCTGATATATT
CTGGGTTATAACTGACCAGCTGTCAACGTGGCTTGCCACCTGCCTCAGCATTTTCTACTT
ACTCAAAATAGCCCACTTCTCCCATCCCCCTTTTCCTTTGGTTGAAGTGGAGATTGAGAGG
AGTGCTTGTTGGTTTTCTTCTATTTTCTTGTTCATTGATTGTTTATTTTCTACTCCT
GGAATTACTGTCTATTTGGGGAGATATTTATGTGATCCCTAAAAGCAATCTGACTTTATA
20 TTCAGAAACAATTAAGACCCTTGCTTTTCAAAGATAATTGTTTTTGATATGCTATATTT
AGTCCCATTTCTTGTGTCCCTAGCCTCATTGCTCCTTTTATTTTTATCCTTGGTGAAGCA
CTCCCAAACCTTGACAGGATTTCTACCACCTCTGAAGATTCCAGAGCCAAGATCCACAA
GAAGGCCATGAAAATGCTATTATCTTTCCTCGTTCTCTTTATAATTCACATTTTTTGCAT
GCAGTTGTCACGGTGGTTATTCTTTTTGTTTCCAAACAACAGGTCAACTAATTTTCTTTT
25 GTTAACATTAAACATCTTCCCATTATCTCATACTTCATTATCATCCTGGGAAACAGCAA
GCTTCGACAAAGAGCAATGAGGGTCCTGCAACATCTTAAAAGCCAACCTTCAAGAGTTGAT
CCTCTCCCTTCATAGATTGTCCAGAGTCTTCACTATGGAAATAGCTTAAAGGGGAGACTT
GGAAGGTCACCTGGTAACTTGTTCTTCCGCTGAGTTCTGTTAAGTAATGCTGGACATATAT
GAACTATCCCTAGTGCATACTGATATT

30

SEQ ID NO:103

Rat T2R14 amino acid sequence

VANIMDWVKRRKLSAVDQLLTVLAI SRITLLWSLYILKSTFSMVPNFEVAIPSTRLTNLV
WIIISNHFN

5 **SEQ ID NO:104**

Rat T2R14 nucleotide sequence

CTGTGGCAAACATAATGGATTGGGTCAAGAGAAGGAAGCTCTCTGCAGTGGATCAGCTCC
TCACTGTGCTGGCCATCTCCAGAATCACTCTGTTGTGGTCATTGTACATACTGAAATCAA
10 CATTTTCAATGGTGCCAACTTTGAGGTAGCTATACCGTCAACAAGACTAACTAATCTTG
TCTGGATAATTTCTAACCATTTTAAT

SEQ ID NO:105

15 Mouse T2R01 amino acid sequence

MQHLLKTIFVICHSTLAIILIFELIIGILGNGFMALVHCMDWVKRKKMSLVN KILTALAI
SRIFHLSLLLSLVIFFSYSDIPMTSRMTQVSNNVWIIIVNHFSIWLSTCLSVLYFLKISN
FSNSFFLYLKWRVEKVVSVTLLVSLLLLILNILLINLEISICIKECQRNISC SFSSHYYA
20 KCHRQVIRLHIIFLSVPVLSLSTFLLLI FSLWTLHQRMQQHVQGGRDARTTAHF KALQT
VIAFFLLYSIFILSVLIQNELLKKNLFVVVFCEVVYIAFPTFHSYILIVGDMKLRQACLP L
CIIAAEIQTTLCRNFRSLKYFRLCCIF

25 **SEQ ID NO:106**

Mouse T2R01 nucleotide sequence

AGCTGTGCGTGAGCAAAGCATTTCTTGTCTGCCACTTCTGAGCTGTGTGAGGAGACACAT
TATCACGGAAAGAGATTCAGACTCTGTCGCTGTCAAACCTGTATGTTTGCTCCTCTTTTA
30 CTGTGAAGGCAGAGTTACGAAAAAAATGTTATGAGAACCAACTCAGAAATTGACAAAAA
TTTTCTAAATGTCATTTTTTAAAATTATATTTCAAATGGAAATGTGAGCAAATCTTTATA
ACTAATATATAAAATGCAGCATCTTTTAAAGACAATATTTGTTATCTGCCATAGCACACT
TGCAATCATTTTAATCTTTGAATTAATAATTGGAATTTTAGGAAATGGGTTCATGGCCCT
GGTGCACTGTATGGACTGGGTTAAGAGAAAGAAAATGTCCTTAGTTAATAAAATCCTCAC

TGCTTTGGCAATCTCCAGAATTTTTCATCTCAGTTTATTGCTTATAAGTTTAGTCATATT
 CTTTTCATATTCTGATATTCCTATGACTTCAAGGATGACACAAGTCAGTAATAATGTTTG
 GATTATAGTCAATCATTTTCAGTATCTGGCTTCTACATGCCTCAGTGTCTTTATTTTCT
 CAAGATATCCAATTTTCTAACTCTTTTTTCTTTATCTAAAGTGGAGAGTTGAAAAAGT
 5 AGTTTCAGTTACACTGTTGGTGTCAATTGCTCCTCCTGATTTTAAATATTTTATTAATTAA
 CTTGGAAATTAGCATATGCATAAAGGAATGTCAAAGAAACATATCATGCAGCTTCAGTTC
 TCATTACTATGCAAAGTGTACAGGCAGGTGATAAGGCTTCACATTATTTTCCTGTCTGT
 CCCC GTTGT TTTGTCCCTGTCAACTTTTCTCCTGCTCATCTTCTCCCTGTGGACACTTCA
 CCAGAGGATGCAGCAGCATGTTTCAGGGAGGCAGAGATGCCAGAACCACGGCCCACTTCAA
 10 AGCCCTACAACTGTGATTGCATTTTCTTACTATATTCATTTTATTCTGTCTGTCTT
 AATACAAATATGAATTACTGAAGAAAATCTTTTCGTTGTATTTTGTGAGGTTGTATATA
 TAGCTTTTCCGACATTCCATTCATATATTCTGATTGTAGGAGACATGAAGCTGAGACAGG
 CCTGCCTGCCTCTCTGTATTATCGCAGCTGAAATTCAGACTACACTATGTAGAAATTTTA
 GATCACTAAAGTACTTTAGATTATGTTGTATATTCTAGACAAAAATTAAGTATACAAAT
 15 GTCTTTTGTATTTTTCATTTTAAATATCCTTTAATTTTGACTGCATGAAATTGATTTCTG
 CTTGCAATTATCACTGATTAAACTATTAATAATTTAACTAGTTGTATACAAGG

SEQ ID NO:107

20 Mouse T2R02 amino acid sequence

MESVLHNFATVLIYVEFIFGNLSNGFIVLSNFLDWVIKQKLSLIDKILLTLAISRITLIW
 EIYAWFKSLYDPSSFLIGIEFQIIYFSWVLSSHFSWLWATTLVVFYLLRIANCSWQIFLY
 LKWRLLKQLIVGMLLGSIVFLLGNLMQSMLEERFYQYGRNTSVNTMSNDLAMWTELIFNM
 25 AMFSVIPFTLALISFLLLIFSLWKHLQKMQLISRRHRDPSTKAHMNALRIMVSFLLLYTM
 HFLSLLISWIAQKHQSELADIIGMITELMYPVHSCILILGNSKLKQTSLCMLRHLRCRL
 KGENITIAYSNQITSFCVFCVANKSMR

30 **SEQ ID NO:108**

Mouse T2R02 nucleotide sequence

CAGCACAGTGAAAACTCATGGGCCACTTGGTCACCCAGGGACAGGCGACGCTGTTATAT
 GCCAAGCTTTCTATGAAC**ATGGAATCTGTCCTTCACAACTTTGCCACTGTACTAATATAC**

GTGGAGTTTATTTTTGGGAATTTGAGCAATGGATTCATAGTGTGTCAAACCTTCTTGGAC
 TGGGTCATTAAACAAAAGCTTTCCTTAATAGATAAAATTCTTCTTACATTGGCAATTTCA
 AGAATCACTCTCATCTGGGAAATATATGCTTGGTTTAAAAGTTTATATGATCCATCTTCC
 TTTTAAATTGGAATAGAATTTCAAATTATTTATTTTAGCTGGGTCCTTCTAGTCACTTC
 5 AGCCTCTGGCTTGCCACAACCTCTCAGCGTCTTTTATTTACTCAGAATAGCTAACTGCTCC
 TGGCAGATCTTCTCTATTTGAAATGGAGACTTAAACAACCTGATTGTGGGGATGTTGCTG
 GGAAGCTTGGTGTCTTGCTTGGAAATCTGATGCAAAGCATGCTTGAAGAGAGGTTCTAT
 CAATATGGAAGGAACACAAGTGTGAATACCATGAGCAATGACCTTGCAATGTGGACCGAG
 CTGATCTTTTTCAACATGGCTATGTTCTCTGTAATACCATTTACATTGGCCTTGATTTCT
 10 TTTCTCCTGCTAATCTTCTCTTTGTGGAAACATCTCCAGAAGATGCAGCTCATTTCCAGA
 AGACACAGAGACCCTAGCACCAAGGCCACATGAATGCCTTGAGAATTATGGTGTCTTTC
 CTCTTGCTCTATACCATGCATTTCTGTCTCTTCTTATATCATGGATTGCTCAAAAGCAT
 CAGAGTGAACCTGGCTGATATTATTGGTATGATAACTGAACTCATGTATCCTTCAGTCCAT
 TCATGTATCCTGATTCTAGGAAATTCTAAATTAAAGCAGACTTCTCTTTGTATGCTGAGG
 15 CATTTGAGATGTAGGCTGAAAGGAGAGAATATCACAAATTGCATATAGCAACCAAATAACT
 AGCTTTTGTGTATTCTGTGTTGCAAACAAATCTATGAGGTAGTTGTTCAAGGAATCCTTC
 CTTGACTTATTGTATCATGGAAGTCATATGGGGGAGTCTGAAAGAGCTGTCTTCTGTAAG
 CAAGGTTTGTATACACTAGTGGGGCTGGGACACCAACCCAAGCACAAAACCTAGCTATAA
 CCTATCCTGGCTGCAGGATATGCTGGAACAATGGTGGCTTGGAAATTGTGGGACTGGCAA
 20 AGCAATAGCTAGTCTAACTTGAGGCCCATTCACACAGCAGGAAGCTCATGCCACCTCTGC
 CTGGATGGCCAGGAAGCAAAATCTTGATGGCCCCAAGACCTATGGTAACTGAACACTAC
 TGAAAAAAGAAAGACTCGTGTTAATGATCTATCAAATATTTCTAATGATATTCTGATAA
 ACTCATATATTAGTCCCTGTCCTAATCATCATCACTGGGACTCCTTCCCAGCACCTGATG
 GGAGCAGATAGAGATCTACATCCAAATAGTAAGTGTATCTTGGGGAACCTCACTTAAGAA
 25 TAGAAGGAACAATTATGAGAGCCAGAGTGATCCAGAACACTAGGATCACAGAATCAACTA
 AGCAGCATGCATAGGGGTAAATGGAGACTGAAGTGGCAATCACAGAGCCTGCATAGGTCT
 AACTAAGTCCTCTGTGTATATACTGTGGCTGTTTAGCTTAGGAATTTTGTGGACTCCT
 AACAATGGATAAGGAATTC

30

SEQ ID NO:109

Mouse T2R03 amino acid sequence

MVLTIRAILWVTLITIISLEFIIGILGNVFIALVNIIDWVKRGKISAVDKTYMALAISRT
 AFLLSLITGFLVSLDLPALLGMRTMVRLLTISWMVTNHFSVWFATCLSIIFYFLKIANFSN
 SIFLVLKWEAKKVVSVTLVVSIIILIMNIIIVINKFTDRLQVNTLQNCSTSNLTKDYGLFL
 FISTGFTLTTPFAVSLTMFLLLIIFSLWRHLKNMCHSATGSRDVSTVAHIKGLQTVVTFLLL
 5 YTAFVMSLLSESLNINIQTNNLLSHFLRSIGVAFPTGHSCVLILGNSKLRQASLSVILWL
 RYKYKHIEHWGP

SEQ ID NO:110

10 Mouse T2R03 nucleotide sequence

CTTTAATAGCAGGGTGTGAATATTTAAATTTTCTTCTGCAGCAACTACTGAGGGCTTCA
 GACTGCTGTATACAGGGCATGAAGCATCTGGATGAAGTTCAGCTGTGCTGCCTTTGACAA
 CAATTTTTTGTGTATGTGTGGAGAACATAAACCATTTCATTAGTGAAATTTGGCTTTTGG
 15 GTGACATTGTCTATGATAGTTCTGAAAGTGATTATGTTAAGAATCAGACACAGCCGTCTA
 GAAGATTGTATTAACACATCTTTGGTAGTTCAGAAGAAATTAGATCATC**CATGGTGTTGAC**
AATAAGGGCTATTTTATGGGTAACATTGATAACTATTATAAGTCTGGAGTTTATCATAGG
AATTTTAGGAAATGTATTCATAGCTCTCGTGAACATCATAGACTGGGTAAAAGAGGAAA
GATCTCTGCAGTGGATAAGACCTATATGGCCCTGGCCATCTCCAGGACTGCTTTTTTATT
 20 **GTCACATAACACAGGGTTCTTGGTATCATTATTGGACCCAGCTTTATTGGGAATGAGAAC**
GATGGTAAGGCTCCTTACTATTTCTTGGATGGTGACCAATCATTTAGTGCTGGTTTGC
AACATGCCTCAGTATCTTTTATTTCTCAAGATAGCTAATTTCTCAAATTCTATTTTCCT
TGTTCTCAAATGGGAAGCTAAAAAGTGGTATCAGTGACATTGGTGGTATCTGTGATAAT
CTTGATCATGAACATTATAGTCATAAACAAATTCAGTACAGACTTCAAGTAAACACACT
 25 **CCAGAACTGTAGTACAAGTAACACTTTAAAAGATTATGGGCTCTTTTATTCATTAGCAC**
TGGGTTTACACTCACCCCATTCGCTGTGTCTTTGACAAATGTTTCTTCTGCTCATCTTCTC
CCTGTGGAGACATCTGAAGAATATGTGTACAGTGCCACAGGCTCCAGAGATGTCAGCAC
AGTGGCCACATAAAAGGCTTGCAAACCTGTGGTAACCTTCCTGTTACTATATACTGCTTT
TGTTATGTCACCTTCTTTCAGAGTCTTTGAATATTAACATTCAACATACAAATCTTCTTTC
 30 **TCATTTTTTTACGGAGTATAGGAGTAGCTTTTCCCACAGGCCACTCCTGTGTACTGATTCT**
TGGAAACAGTAAGCTGAGGCAAGCCTCTCTTCTGTGATATTGTGGCTGAGGTATAAGTA
CAAACATATAGAGAATTGGGGCCCCTAAATCATATCAGGGATCCTTTTCCACATTCTAGA
 AAAAAATCAGTTAATAAGAACAGGAATTTAGGAAGGAATCTGAAATTATGAATCTCATAG
 GCCATGAACCTTCAGACAAAGGATTCATTAGAGAGATAGAGAGAGAACATTGTTATCTGT

AACTCGACAGGCAACACTGTAGATTATGAAAATAAATGTCAGTCTGTAATGGAAAGCAAA
ACATGCTATATTTTATTAATTGGTTTTGGTTTAAGGTCGGGATA

5 **SEQ ID NO:111**

Mouse T2R04 amino acid sequence

MLSALESILLSVATSEAMLGVLGNTFIVLVNYTDWVRNKKLSKINFILTGLAISRIFTIW
IITLDAYTKVFLLTMLMPSSLHECMSYIWVIINHLSVWFSTSLGIFYFLKIANFSHYIFL
10 WMKRRADKV FVFLIVFLIITWLASFPLAVKVIKDVKIYQSNTSWLIHLEKSELLINYVFA
NMGPISLFI VAI IACFLLTISLWRHSRQMQSIGSGFRDLNTEAHMKAMKVLI AFIIILFIL
YFLGIL IETLCLFLTNKLLFIFGFTLSAMYPCCHSFILILTSRELKQDTMRALQRLKCC
ET

15

SEQ ID NO:112

Mouse T2R04 nucleotide sequence

CTGCAGCAGGTAAATCACACCAGATCCAGCAGAAGCCTTCTTGGA AATTGGCAGAGATGC
20 TGAGTGC ACTGGAAAGCATCCTCCTTTCTGTTGCCACTAGTGAAGCCATGCTGGGAGTTT
TAGGGAACACATTTATTGTACTTGTA AACTACACAGACTGGGTCAGGAATAAGAACTCT
CTAAGATTA ACTTTATTCTCACTGGCTTAGCAATTTCCAGGATTTTACCATATGGATAA
TAACTTTAGATGCATATACAAAGGTTTTCTTCTGACTATGCTTATGCCGAGCAGTCTAC
ATGAATGCATGAGTTACATATGGGTAATTATTAACCATCTGAGCGTTTGGTTTAGCACCA
25 GCCTCGGCATCTTTTATTTTCTGAAGATAGCAAATTTTCCCACTACATATTTCTCTGGA
TGAAGAGAAGAGCTGATAAAGTTTTTGTCTTTCTAATTGTATTCTTAATTATAACGTGGC
TAGCTTCCTTTCCGCTAGCTGTGAAGGTCATTAAAGATGTTAAAATATATCAGAGCAACA
CATCCTGGCTGATCCACCTGGAGAAGAGTGAGTTACTTATAAACTATGTTTTTGCCAATA
TGGGGCCCATTTCCCTCTTTATTGTAGCCATAATTGCTTGTTTCTTGTTAACCATTTCCC
30 TTTGGAGACACAGCAGGCAGATGCAATCCATTGGATCAGGATTCAGAGATCTCAACACAG
AAGCTCACATGAAAGCCATGAAAGTTTTAATTGCATTTATCATCCTCTTTATCTTATATT
TTTTGGGTATTCTCATAGAAACATTATGCTTGTTTCTTACAAACAATAAACTTCTCTTTA
TTTTTGGCTTCACCTTGTCAGCCATGTATCCCTGTTGCCATTCCTTTATCCTAATTCTAA
CAAGCAGGGAGCTGAAGCAAGACACTATGAGGGCACTGCAGAGATTAAATGCTGTGAGA

CTTGACAGAGAAATGAATGTTCTGGCACAGTTCAGCAGGGAATCCCTGGAGCCCTTTCCA
 TTCCCACACTATGTTCTCACACTGTCTTTAGTTGAATTGTTAAAAGTTTTTGAAACCTTTGG
 CAACTGATTGACTGCAGCTACGCCAGTGTAAGATTTTCATAGTAAGAGCAAACATTGAAA
 ATAAGACTTCTCAGTCTTATTTTCATTGAGTTTCTAAAGCATTGACACCCATTACCCAGAA
 5 AAACCAAAGGGGAAGAGAGGAGTTTTTCAGACATGTGTGATGAATCTTGATATTTAGGACA
 TGGAATTGAGGAG~CCAGAGGGATGCTACCGTGTGTCTACAGCTTTGTTTGTTAAATAGC
 TACTTTTCCTTTCCAGTTAGTTAAAGTAGATGCTTGGAGTAGTGGTGAAAATCATGGCA
 GTAGATGGGATCTGTGGGAAGTGGTTGAGGAAGCAGGCTGTTTCTGAACGAAGAGACCAG
 AGGACTGATTGAACTGGTCATTGTGTATATCAAAAATAGTGATTTTCAGATGAAGCCAAGT
 10 TGTAGAGCAAAGATATCTGAGGAAGAATTC

SEQ ID NO:113

Mouse T2R05 amino acid sequence

15 MLSAATEGILLSIATVEAGLGVLGNTFIALVNCMDWAKNNKLSMT**T**GFLLI GLATSRI FIVW
 LLTLDAYAKLFYPSKYFSSSLIEI**I**SYIWMTVNHLTVWFATSLSIFYFLKIANFSDCVFL
 WLKRRTDKAFVFLGCLL**T**SWVISFSFVVKVMKD**G**KVNHRNRTSEMYWEKRQFTINYVFL
 NIGVISLFMMTLTACFLLIMSLWRHSRQM QSGVSGFRDLNTEAHVKAIKFLISFIILFVL
 20 YFIGVSIIEIICIFIPENKLLFIFGFTTASIYPCCHSFILILSNSQLKQAFVKVL**L**QGLKFF

SEQ ID NO:114

Mouse T2R05 nucleotide sequence

25 **ATGCTGAGTGC**GGCAGAAAGGCATCCTCCTTTCCATTGCAACTGTTGAAGCTGGGCTGGGA
GTTTTAGGGAACACATTTATTGCACTGGTAAACTGCATGGACTGGGCCAAGAACAATAAG
CCTTCTATGACTGGCTTCCTTCTCATCGGCTTAGCAACTTCAGGATTTTTATTGTGTGG
CTATTAACCTTTAGATGCATATGCAAAGCTATTCTATCCAAGTAAGTATTTTTCTAGTAGT
 30 **CTGATTGAAATCATCTCTTATATATGGATGACTGTGAATCACCTGACTGTCTGGTTTGCC**
ACCAGCCTAAGCATCTTCTATTTCTGAAGATAGCCAATTTTTCCGACTGTGTATTTCTC
TGGTTGAAGAGGAGAACTGATAAAGCTTTTGTTTTTCTCTTGGGGTGTTTGCTAACTTCA
TGGGTAAATCTCCTTCTCATTTGTTGTGAAGGTGATGAAGGACGGTAAAGTGAATCATAGA
AACAGGACCTCGGAGATGTACTGGGAGAAAAGGCAATTCCTATTAACCTACGTTTTCTC

AATATTGGAGTCATTTCTCTCTTTATGATGACCTTAACTGCATGTTTCTTGTTAATTATG
 TCACTTTGGAGACACAGCAGGCAGATGCAGTCTGGTGTTTCAGGATTCAGAGACCTCAAC
 ACAGAAGCTCATGTGAAAGCCATAAAATTTTAATTTCAATTTATCATCCTTTTCGTCTTG
 TATTTTATAGGTGTTTCAATAGAAATTATCTGCATATTTATAACCAGAAAACAACTGCTA
 5 TTTATTTTGGTTTCACAACTGCATCCATATATCCTTGCTGTCACTCATTTATTCTAATT
 CTATCTAACAGCCAGCTAAAGCAAGCCTTTGTAAAGGTACTGCAAGGATTAAAGTTCTTT
 TAG

10 **SEQ ID NO:115**

Mouse T2R06 amino acid sequence

MLTVAEGILLCFVTSGSVLGVLGNGFILHANYINCVRKKFSTAGFILTGLAICRIFVICI
 IISDGYLKLFSPhMVASDAHIIVISYIWVIINHTSIWFATSLNLFYLLKIANFSHYIFFC
 15 LKRRINTVFIFLLGCLFISWSIAFPQTVKIFNVKKQHRNVSWQVYLYKNEFIVSHILLNL
 GVIFFFMVAIITCFLLIISLWKHNRKMQLYASRFKSLNTEVHVKVMKVLISFIIILLILHF
 IGILIETLSFLKYENKLLILGLIISCMYPCCHSFILILANSQKQASLKALKQLKCHKK
 DKDVRVTW

20

SEQ ID NO:116

Mouse T2R06 nucleotide sequence

TATAGTTGCAGCAGAAGCAACGTTAGGGATCTGTAGAGATGCTGACTGTAGCAGAAGGAA
 25 TCCTCCTTTGTTTTGTAAGTAGTGGTTCAGTCCTGGGAGTTCTAGGAAATGGATTTATCC
 TGCATGCAAACTACATTAAGTGTGTCAGAAAGAAGTTCTCCACAGCTGGCTTTATTCTCA
 CAGGCTTGGCTATTTGCAGAAATCTTTGTCATATGTATAATAATCTCTGATGGATATTTAA
 AATTGTTTTCTCCACATATGGTTGCCTCTGATGCCACATTATAGTGATTCTTACATAT
 GGGTAATTATCAATCATAAAGTATATGGTTTGCCACCAGCCTCAACCTCTTCTATCTCC
 30 TGAAGATAGCAAATTTTCTCACTACATCTTCTTCTGCTTGAAGAGAAGAATCAATACAG
 TATTTATCTTTCTCCTGGGATGCTTATTTATATCATGGTCAATTGCTTTCCACAAACAG
 TGAAGATATTTAATGTTAAAAGCAGCACAGAAaTGTTTCCTGGCAGGTTTACCTCTATA
 AGAATGAGTTCATtGTAAGCCACATTCTTCTCAACCTGGGAGTTATATTCTTCTTTATGG
 TGGCTATCATTACATGCTTCCTATTAATTATTTCACTTTGGAAACATAACAGAAAGATGC

AGTTGTATGCCTCAAGATTCAAAGCCTTAACACAGAAGTACATGTGAAAGTCATGAAAG
 TTTTAATTTCTTTTATTATCCTGTTAATCTTGCATTTTCATAGGGATTTTGATAGAAACAT
 TGAGCTTTTTAAAATATGAAAATAAACTGCTACTTATTTTGGGTTTGATAATTCATGCA
 TGTATCCTTGCTGTCATTCATTTATCCTAATTCTAGCAAACAGTCAGCTGAAGCAGGCTT
 5 CTTTGAAGGCACTGAAGCAATTAAAATGCCATAAGAAAGACAAGGACGTCaAGTGACAT
 GGTAGACTTATGGAGAAATGAATGGTCACAAGAAATAGCCTGGTGTGGAGATGTTGATAT
 CTCTAAAGACCGTTTCACTTCCAAATTCTTGCAATTATTTAAAAAAAAGTCTTGCTGA
 TATCATGGAATCATGGGAAATGTTGCAATTGTGTTTTGGGGACAGGGTGACCAGTGAAGG
 TATGGTTAAGCAGCGAAACACTCATAACAGCTCGTTCGTTCTTTTGTATTTTATTTTGTG
 10 TTGGTGGCCTTCCAAGACATGATTTCTCTATGTAAGTTTTGG

SEQ ID NO:117

Mouse T2R07 amino acid sequence

15 MLNSAEGILLCVVTSEAVLGVLGDYIALFNCMDYAKNKKLSKIGFILIGLAISRIGVW
 I IILQGYIQVFFPHMLTSGNITEYITYIWVFLNHLVWFVTNLNILYFLKIANFSNSVFL
 WLKRRVNAVFIIFLSGCLLTSWLLCFPQMTKILQNSKMHQRNTSWVHQRKNYFLINQSVTN
 LGIFFFIIVSLITCFLLVFLWRHVRQMHSVDVSGFRDHSTKVHV KAMKFLISFMVFFILH
 20 FVGLSIEVLCFILPQNKLLFITGLTATCLYPCGHSIIVILGNKQLKQASLKALQQLKCCE
 TKG NFRVK

SEQ ID NO:118

25 Mouse T2R07 nucleotide sequence

TTCATAATGAAGAGGAGGCAGGGCAATGTTGGTTTCTGTTGTCTGACCAGTGTATTTGAC
 AGTGATACTACACATTTGATTGCTAAATGCAAATAGTTCCAAAGGAACAAGTAAATTTTA
 TGAAATAGAAGCTTCTATTTGCTTATTAACAAACTGCAAGCAAACATTAGTCTGCACACA
 30 TTTTATAGACAAGCTAAATCTTCAAAGCAATAAAAAAGAGCACCCATAAAGTTCTGACT
 CTATCACATGACAATAGGCTTGAAAAGATTGTCTATGTAGATAAAGAAGATGGCATAACT
 TCTCCATCAAGAAGCCAGTATATGGGACATTCTCCAGCAGATAATTTACAATAGATGCAG
 CAGAAGTAACCTTAGAGATCTGTAAAG**ATGCTGAATTCAGCAGAAGGCATCCTCCTTTGT**
GTTGTCACTAGTGAGGCTGTGCTCGGAGTTTTAGGGGACACATATATTGCACCTTTTTAAC

TGCATGGACTATGCTAAGAACAAGAAGCTCTCTAAGATCGGTTTCATTCTCATTGGCTTG
 GCGATTTCCAGAATTGGTGTGTATGGATAATAATTTTACAAGGGTATATACAAGTATTT
 TTTCCACACATGCTTACCTCTGGAAACATAACTGAATATATTACTTACATATGGGTATTT
 CTCAATCACTTAAGTGTCTGGTTTGTACCAACCTCAACATCCTCTACTTTCTAAAGATA
 5 GCTAATTTTTCCAACCTCTGTATTTCTCTGGCTGAAAAGGAGAGTCAATGCAGTTTTTATC
 TTTCTGTCAGGATGCTTACTTACCTCATGGTACTATGTTTTCCACAAATGACAAAGATA
 CTTCAAAATAGTAAAATGCACCAGAGAAACACATCTTGGGTCCACCAGCGGAAAAATTAC
 TTTCTTATTAACCAAAGTGTGACCAATCTGGGAATCTTTTTCTTCATTATTGTATCCCTG
 ATTACCTGCTTTCTGTTGATTGTTTTCTCTGGAGACATGTCAGACAAATGCACTCAGAT
 10 GTTTCAGGATTCAGAGACCACAGCACAAAAGTACATGTGAAAGCTATGAAATTTCTAATA
 TCTTTTATGGTCTTCTTTATTCTGCATTTTGTAGGCCTTTCCATAGAAGTGCTATGCTTT
 ATTCTGCCACAAAATAAACTGCTCTTTATAACTGGTTTGACAGCCACATGCCTCTATCCC
 TCGGGTCACTCAATCATCGTAATTTTAGGAAATAAGCAGTTAAAGCAAGCCTCTTTGAAG
 GCACTGCAGCAACTAAAATGCTGTGAGACAAAAGGAAATTCAGAGTCAAATAAATGGGT
 15 TTGCAAATAAATAGCTGCCTTGTTCTTcCACTGGTTTTTACCCTGTTAGTTGATGTTATG
 AAAAGTTCCCTGCTATGGTTGATGACATCTCAAGGAATCTATTTTTCTGGTGGCATGTTAA
 GTCCACGTGAAGCCTCACTTCATACTGTGACTTGACTATGCAAATTCCTTCCACAAAATA
 ACCAGATAACATTCAGCCTGGAGATAAATTCATTTAAAGGCTTTTATGGTGAGGATAAAC
 AAAAAAAAAAATCATTTTTCTGTGATTCACTGTAACTCCCAGGATGAGTAAAAGAAAAC
 20 AAGACAAATGGTTGTGATCAGCCTTTGTGTGTCTAGACAGAGCTAGGGACCAGATGTTGA
 TGCTTGTGTGTGGTTTTGAGTTCTTTAAGAAGTTATTGCCTCTCTGCCATTCGGTATTCC
 TCAGGTGAGAATTC

25 **SEQ ID NO:119**

Mouse T2R08 amino acid sequence

MLWELYVFVFAASVFLNFVGIIANLFIIVIIIKTWVNSRRIASPDRLIFSLAITRFLTLG
 LFLNLSVYIATNTGRSVYFSTFLLCWKFLDANSLWLVTILNSLYCVKITNFQHPVFLLL
 30 KRTISMKTTSLLLACLLISALTLLLYMLSQISRFEHIIGRNDTSFDLSDGILTLVASL
 VLNSLLQFMLNVTFASLLIHSLRRHIQKMQRNRTSFWNPQTEAHMGAMRLMICFLVLYIP
 YSIATLLYLPSYMRKNLRAQAICMIITAAYPPGHSVLLIITHHKLKAKAKKIFCFYK

SEQ ID NO:120

Mouse T2R08 nucleotide sequence

AAGCTTGTTTGTAATTAGGCATTCCCTAAGAAAATAAGAACAGGAGTGAAGAAATAGTAAT
5 TTAATCCTTGAAAGATTTGCATCTCAGTAAAAGCAGCTGCCTCTTAGACCAGAAATGGTG
TTTGCCATGCTGGAAAATAAAAAGGAGACCTCTTTCCAGGCTGCATCCTGTGTCTGCTTA
CTTATTTTCAGTTTGTTCATCGGCACCAAACGAGGAAAG**ATGCTCTGGGAACTGTATGT**
ATTTGTGTTTGCTGCCTCGGTTTTTTTAAATTTTGTAGGAATCATTGCAAATCTATTTAT
TATAGTGATAATTATTAAGACTTGGGTCAACAGTCGCAGAATTGCCTCTCCGGATAGGAT
10 **CCTGTTTCAGCTTGGCCATCACTAGATTCTGACTTTGGGGTTGTTTCTACTGAACAGTGT**
CTACATTGCTACAAATACTGGAAGGTCAGTCTACTTTTCCACATTTTTTCTATTGTGTG
GAAGTTTCTGGATGCAAACAGTCTCTGGTTAGTGACCATTCTGAACAGCTTGTATTGTGT
GAAGATTACTAATTTTCAACACCCAGTGTTTCTCCTGTTGAAACGGACTATCTCTATGAA
GACCACCAGCCTGCTGTTGGCCTGTCTTCTGATTTTCAGCCCTCACCCTCTCCTATATTA
15 **TATGCTCTCACAGATATCACGTTTTCTGAACACATAATTGGGAGAAATGACACGTCATT**
TGACCTCAGTGATGGTATCTTGACGTTAGTAGCCTCTTTGGTCCTGAACTCACTTCTACA
GTTTATGCTCAATGTGACTTTTGCTTCCTTGTTAATACATTCTTGAGAAGACATATACA
GAAGATGCAGAGAAACAGGACCAGCTTTTGGAAATCCCCAGACGGAGGCTCACATGGGTGC
TATGAGGCTGATGATCTGTTTCCTCGTGCTCTACATTCCATATTCAATTGCTACCCTGCT
20 **CTATCTTCCTTCCTATATGAGGAAGAATCTGAGAGCCCAGGCCATTTGCATGATTATTAC**
TGCTGCTTACCCTCCAGGACATTCTGTCCTCCTCATTATCACACATCATAACTGAAAGC
TAAAGCAAAGAAGATTTTCTGTTTCTACAAGTAGCAGAATTTCATTAGTAGTTAACAGCA
TCAATTCATGGTTTGGTTGCATTAGAAATGTCTCAGTGATCTAAGGACTTAATTTTGTGA
TCTTGATCTGGCATCCTGACCCTGAGACTAAGTGCTTATATTTTGGTCAATACAGCATC
25 TTTTGGCTAATATTTTAAAGTAAATCACATTCCATAAGAAATTGTTTAAGGGATTACGT
ATTTTTCATGGCTATCACATTCCCTAGACAATGGAAATCACCATACTGTTTCGCTAGCTAC
TGAAGTACCAGGGGAAAGTCCATGAATGAAGGCCACATTGTGATGTTCTTGTTAGCACA
GATTAGAGAATTTGGCCTCAACTGAGCAAGATATC

30

SEQ ID NO:121

Mouse T2R09 amino acid sequence

MEHLLKRTFDITENILLIILFIELIIGLIGNGFTALVHCMDWVKRKKMSLVNKKILTALAT
 SRIFLLWFMLVGFPISSLYPYLVTTRLMIQFTSTLWTIANHISVWFATCLSVFYFLKIAN
 FSNPFLYLKRRVEKVSVTLLVSLVLLFLNILLNLEINMCINEYHQINISYIFISYYH
 LSCQIQVLGSHIIFLSVPVLSLSTFLLLIIFSLWTLHKRMQQHVQGGRDARTTAHFKALQ
 5 AVIAFLLLYSIFILSLLLQFWIHGLRKKPPFIAFCQVVDTAFPSFHSYVLILRDRKLRHA
 SLSVLSWLKCRPNYVK

SEQ ID NO:122

10 Mouse T2R09 nucleotide sequence

GAATTCAGAAATCATCAAAAAATCTTCAAACTACATGTTTAAAATAGCACTTCAAATGA
 ATACATTTGCAAATCTTTACAATAACATAAAATGGAGCATCTTTTGAAGAGAACATT
TGATATCACCGAGAACATACTTCTAATTATTTTATTCATTGAATTAATAATTGGACTTAT
 15 **AGGAAACGGATTCACAGCCTTGGTGCCTGCTGCTGGGTTAAGAGAAAAAAATGTC**
ATTAGTTAATAAAATCCTCACCGCTTTGGCAACTTCTAGAATTTTCCTGCTCTGGTTCAT
GCTAGTAGGTTTCCAATTAGCTCACTGTACCCATATTTAGTTACTACTAGACTGATGAT
ACAGTTCACTAGTACTCTATGGACTATAGCTAACCATATTAGTGTCTGGTTTGCTACATG
CCTCAGTGTCTTTTATTTTCTCAAGATAGCCAATTTTCTAATTCTCCTTTTCTCTATCT
 20 **AAAGAGGAGAGTTGAAAAAGTAGTTTCAGTTACATTACTGGTGTCTCTGGTCCTCTTGTT**
TTTAAATATTTTACTACTTAATTTGGAAATTAACATGTGTATAAATGAATATCATCAAT
AAACATATCATACTCTTCATTTCTTATTACCATTTAAGTTGTCAAATTCAGGTGTTAGG
AAGTCACATTATTTTCTGTCTGTCCCGTTGTTTGTCCCTGTCAACTTTTCTCCTGCT
CATCTTCTCCCTGTGGACACTTCACAAGAGGATGCAGCAGCATGTTCAAGGAGGCAGAGA
 25 **TGCCAGAACCACGGCCCACTTCAAAGCCTTGCAAGCAGTGATTGCCTTTCTCCTACTATA**
CTCCATTTTTTATCCTGTCACTGTTACTACAATTTTGGATCCATGGATTAAGGAAGAAACC
TCCTTTCATTGCATTTTGTGAGGTTGTAGATACAGCTTTTCTTTCATTCCATTCATATGT
CTTGATTCTGAGAGACAGGAAGCTGAGACACGCCTCTCTCTGTGTTGTGCTGGCTGAA
ATGCAGGCCAAATTATGTGAAATAATATTTCTTGTATTTTCATTTTCAATTTTAAATA
 30 **TTCTTAGAATTTGACTGCATGTATTTTATCTTTTATTTGAAACAACCACTAATTAAAGCT**
ATTACTAATTTAGCAAGTCGTATACAAGGTTATTTTTTAATACACATATCAAAAACCTGAC
ATGTTTATGTTCTACAAAACCTGAATATATCAAAATTATATAAATTTGTATCAACGAT
TAACAATGGAGTTTTTTTATTTATGACCTGTCACGGGACTCCGGTGGAGTCAGCTTGTCA
GATGAAAGTCTGAAAGCTT

[illegible]

5

10

15

20

25

AGGAATGTTGAGCCTTAGGTTGATAGGAGGAAAATTAATACTTTTATTTGACCACATTTT
 TGAATAGGTTTTCTATAAGCCACTCATTTGTGCTGATTCTGGGAAATAACAAGCTGAG
 ACAAGCCAGTCTTTCAGTGTTCATTGTCTGAGGTGCCGATCCAAAGATATGGACACCAT
 GGGTCCATAAAAAATTTTCTAGAGGTCATTGGGAAACATTTTCTAGATCTTATAGGGGAAAAA
 5 GAAAATGTGGGGCTTCAAAGCTGGTAGGAGTAATATAGAGAAGGATAGGAG

SEQ ID NO:125

Mouse T2R11 amino acid sequence

10 MEHPLRRTFDFSQSILLTILFIELIIGLIRNGLMVLVHCIDWVKRKKFHLLIKSSPLWQT
 SRICLLWFMLIHLLITLLYADLASTRMMQFASNPWTISNHISIWLATCLGVFYFLKIAN
 FSNSTFLYLKWRVQFLLLNILLVKFEINMWINEYHQINIPYSFISYYQXCQIQVLSLHI
 FLSVPFILSLSTFLLLIIFSLWTLHQRMQQHVQGYRDASTMAHFKALQAVIAFLLIHSIFI
 15 LLLLLQLWKHELKRPFPVFCQVAYIAFPSSHSYVFILGDRKLRQACLSVLWRLKCRPN
 YVG

SEQ ID NO:126

20 Mouse T2R11 nucleotide sequence

AATAATGTATGTGGAAGAGTTAAGTATAAATGTTGTATGAGAATGAACTCAGAAATCATC
 AAAAATCTTTAAACTGCATGTTAAAAATCACACTTCAAATGAATATATTTGTAATTCTT
 TAGAACTAATAAATAAAATGGAGCATCCTTTGAGGAGAACATTTGATTTCTCCAGAGCA
 25 TACTTCTAACCATTTTATTCATTGAATTAATAATTGGACTTATAAGAAATGGATTAATGG
 TATTGGTGCACCTGCATAGATTGGGTAAAGAGAAAAAATTTTCAATTTGTTAATCAAATCCT
 CACCACCTTTGGCAAATTCAGAAATTTGTCTGCTCTGGTTCATGCTAATACATCTCCTGA
 TTACTTTATTGTATGCAGATTTAGCTAGTACTAGAACGATGATGCAATTCGCTAGCAATC
 CATGGACTATATCTAACCATATCAGCATCTGGCTTGCTACATGCCTTGGTGTCTTTTATT
 30 TTCTCAAGATAGCCAATTTTCTAACTCTACTTTTCTCTATCTAAAATGGCGAGTTCAGT
 TCCTCTTGTTAAATATTTTACTGGTTAAATTTGAGATTAACATGTGGATAAATGAATATC
 ATCAAATAAACATACCATACAGCTTCATTTCTTATTACCAAATTGTCAAATACAGGTGTT
 AAGTCTTCACATTATTTTCTGTCTGTCCCTTTATTTTGTCCCTGTCAACTTTTCTCCT
 GCTCATCTTCTCCCTGTGGACACTTCACCAGAGGATGCAGCAGCATGTTCAAGGATACAG

AGATGCCAGCACAAATGGCCCACTTCAAAGCCTTGCAAGCAGTGATTGCCTTTCTCTTAAT
 ACACTCCATTTTTATCCTGTCACTGTTACTACAACCTTTGGAAACATGAATTAAGGAAGAA
 ACCTCCTTTTGTGTATTTTGTGAGGTTGCATATATAGCTTTTCCTTCATCCCATTCTATA
 TGTCTTCATTCTGGGAGACAGAAAGCTGAGACAGGCTTGTCTCTCTGTGTTGTGGAGGCT
 5 GAAATGCAGGCCAAATTATGTGGGATAAAATCTCTTTGTGCTTTCATTTCGAATTCTTAA
 ATATTCTTTGATTTTGAATGCATAAATT

SEQ ID NO:127

10 Mouse T2R12 amino acid sequence

GAIVNVDFLIGNVGNFIVVANIMDLVKRRKLSSVDQLLTALAVSRITLLWYLYIMKRTE
 LVDPNIGAIMQSTRLTNVIWIISNHFSIWLATTLISIFYFLKIANFNSNIFCYLRWRFEKV
 ILMALLVSLVLLFIDILVTNMYINIWTDEF

15

SEQ ID NO:128

Mouse T2R12 nucleotide sequence

20 TTTTCAGCAGTGACTTTGGGAAGCAGAACGTCCTCTTAGAGACAGTGGGTGCTGCTATCC
 TAGTTAATGTGGAGCAATAGTTAATGTGGATTTCTTAATTGGAAATGTTGGGAATGGATT
 CATTGTTGTGGCAAACATAATGGACTTGGTCAAGAGAAGAAAGCTTTCTTCAGTGGATCA
 GCTGCTCACTGCACTGGCCGTCTCCAGAATCACTTTGCTGTGGTACCTGTACATAATGAA
 ACGAACATTTTTAGTGGATCCAAACATTGGTGAATTATGCAATCAACAAGACTGACTAA
 25 TGTTATCTGGATAATTTCTAACCATTTTAGTATATGGCTGGCCACCACCCTCAGCATCTT
 TTATTTTCTCAAGATAGCAAATTTTCTAACTCTATTTTCTGTTACCTGAGGTGGAGATT
 TGAAAAGGTGATTTTGATGGCATTGCTGGTGTCCCTGGTCCTCTTGTTTATAGATATTTT
 AGTAACAAACATGTACATTAATATTTGGACTGATGAATTC

30

SEQ ID NO:129

Mouse T2R13 amino acid sequence

MVAVLQSTLPPIIFSMEFIMGTLGNGFIFLIVCIDWVQRRKISLVDQIRTA LAISRIALIW
LIFLDWWVSVHYPALHETGKMLSTYLISWTVINHCNFWLTANLSILYFLKIANFSNII FL
YLKFRSKNVVLVTLLVSLFFLFLNTVIIKIFSDVCFDSVQRNVSQIFIMYNHEQICKFLS
FTNPMFTFIPFVMSTVMFSLLI FSLWRHLKNMQHTAKGCRDISTTVHIRALQTIIVSVVL
5 YTIFFLSFFVKVWSFVSPERYLIFLFVWALGNAVFSAHPFVMILVNRRLRLASLSLIFWL
WYRFKNIEV

SEQ ID NO:130

10 Mouse T2R13 nucleotide sequence

AAGCTTGTGTTGTGTTTGGATGAATTCTATTTATGTCTATCAATTTAAGATTTTCATATGA
ATCATTAAAGAAATCTTGATAGTTGTTTGTGAGATATCACTTCTGCAATTTTTTAAATGAAA
TTACACTCATATTTTGAAGGAACAATATGTTTTAAAGGAATATATTAACAAATCTTCAGC
15 AGTTACCTCAGAAGTTTGGGTATTGTTTTACAGAAAATGGTGGCAGTTCTACAGAGCACA
CTTCCAATAATTTTCAGTATGGAATTCATAATGGGAACCTTAGGAAATGGATTCATTTTT
CTGATAGTCTGCATAGACTGGGTCCAAAGAAGAAAAATCTCTTTAGTGGATCAAATCCGC
ACTGCTCTGGCAATTAGCAGAATCGCTCTAATTTGGTTGATATTCCTAGATTGGTGGGTG
TCTGTTCAATTACCCAGCATTACATGAAACTGGTAAGATGTTATCAACATATTTGATTTCC
20 TGGACGGTGATCAATCATTTGTAACTTTTGGCTTACTGCAAACCTTGAGCATCCTTTATTTT
CTCAAGATAGCCAACTTTTCTAACATTATTTTTCTTTATCTAAAGTTTAGATCTAAAAAT
GTGGTATTAGTGACCCTGTTAGTGTCTCTATTTTTCTTGTTCTTAAATACTGTAATTATA
AAAATATTTTCTGATGTGTGTTTTGATAGTGTTCAAAGAAATGTGTCTCAAATTTTCATA
ATGTATAACCATGAACAAATTTGTAAATTTCTTTCCTTTACTAACCCTATGTTACATTC
25 ATACCTTTTGTATGTCCACGGTAATGTTTTCTTTGCTCATCTTCTCCCTGTGGAGACAT
CTGAAGAATATGCAGCACACCGCCAAAGGATGCAGAGACATCAGCACCACAGTGCACATC
AGAGCCCTGCAAACCATCATTGTGTCTGTAGTGCTATACACTATTTTTTTTTCTATCATTT
TTTGTTAAAGTTTGGAGTTTTGTGTCAACAGAGAGATACCTGATCTTTTTGTTTGTCTGG
GCTCTGGGAAATGCTGTTTTTTCTGCTCACCCATTTGTCATGATTTTGGTAAACAGAAGA
30 TTGAGATTGGCTTCTCTCTCTGATTTTTTGGCTCTGGTACAGGTTTAAAAATATAGAA
GTATAGGGTCCAAAGACCACCAAGGAATCATTTTCCTTATCCTAAAGAAAAATCAGGAG

SEQ ID NO:131

Mouse T2R14 amino acid sequence

MLSTMEGVLLSVSTSEAVLGIVGNTFIALVNCMDYNRNKKLSNIGFILTGLAISRICLVL
ILITEAYIKIFYPQLLSPVNIIEELISYLVWIIICQLNVWFATSLSIFYFLKIANFSHYIFV
5 WLKRRIDLVFFFLIGCLLISWLFSPVVAKMVKDNKMLYINTSWQIHMKKSELIINYVFT
NGGVFLFFMIMLIVCFLLIISLWRHRRQMESNKLGFRLNTEVHVRTIKVLLSFIILFIL
HFMGITINVICLLIPESNLLFMFGLTTAFIYPGCHSLILILANSRLKQCSVMILQLLKCC
ENGKELRDT

10

SEQ ID NO:132

Mouse T2R14 nucleotide sequence

CTGCAGGTATATACCTACCCTGAAGGCTTCATCTAGAGTAAACAAAGTAGTCTGTATAGT
15 CTGCCATTCCTCAGATTCTCCTCAACTTCCCACCCTCCAGTGACCTTTCTCCTTTTCTAC
AGTCAAACATATGGACCTCACAACCTGACACTTCTTCAGATGCAAAATATTCTCACAGAGA
CAAGTAAACATACAAAACAAATACTTTAATTTGCCTATTAACAAATGGCAAGAAAAGAT
TCAGGCTTGAACATCCTGTAGACAAGCTAAGGACAGGAGCAACTGAAGGGATCTCCATGA
AGACCTTTCAGATTTCTACCAAAGTAATTTTAACTATATTTAAGTCTTTAAAGAAAGA
20 AAGTAAAGCCACTCTTTTATTGAACAGCAATAGATTGGAATCTTAAACAACTGCAACAGA
AGCCATTTTAAAGATCAACAAAGATGCTGAGCACAAATGGAAGGTGTCCTCCTTTCAGTTT
CAACTAGTGAGGCTGTGCTGGGCATTGTAGGGAACACATTCATTGCACTTGTAACCTGTA
TGGACTATAACAGGAACAAGAAGCTCTCTAATATTGGCTTTATTCTCACTGGCTTGGCAA
TTTCCAGAATTTGCCTTGTGTTGATCTTAATCACAGAGGCATACATAAAAATATTCTATC
25 CACAGTTGCTGTCTCCTGTCAACATAATTGAGCTCATCAGTTATCTATGGATAATTATCT
GTCAATTGAATGTCTGGTTTGCCACTAGTCTCAGTATTTTTTATTTCCTGAAGATAGCAA
ATTTTTCCCACTACATATTTGTCTGGTTAAAAAGAAGAATTGATTTAGTTTTTTTCTTCC
TGATAGGGTGCTTGCTTATCTCATGGCTATTTTCTTTCCAGTTGTTGCGAAGATGGTTA
AAGATAATAAAATGCTGTATATAAACACATCTTGGCAGATCCACATGAAGAAAAGTGAGT
30 TAATCATTAACATATGTTTTACCAATGGGGGAGTATTTTTATTTTTTATGATAATGTTAA
TTGTATGTTTCCTGTTAATCATTTCACTTTGGAGACATCGCAGGCAGATGGAATCAAATA
AATTAGGATTCAGAGATCTCAACACAGAAGTTCATGTGAGAACAAATAAAAGTTTTATTGT
CTTTTATTATCCTTTTTTATATTGCATTTTCATGGGTATTACCATAAATGTAATTTGTCTGT
TAATCCCAGAAAGCAACTTGTTATTCATGTTTGGTTTGACAACTGCATTCATCTATCCCG

GCTGCCACTCACTTATCCTAATTCTAGCAAACAGTCGGCTGAAGCAGTGCTCTGTAATGA
TACTGCAACTATTAAAGTGCTGTGAGAATGGTAAAGAACTCAGAGACACATGACAGTCTG
GAACACATGCAATCTGGAATTGTCAGTGGAAGTTACTGAAGATCTTTTCACTTGAC
TATGCTCTTTTATTGATTTGGCATCATTATCAAACACTGTTGGAGCCTTGTGAACTCTTG
5 TTCAGAGTCTTCTGCCTCTCAAGGAATCACACTCC

SEQ ID NO:133

Mouse T2R15 amino acid sequence

10 MCAVLRSLTIIIFILEFFIGNLGNGFIALVQCMDLRKRRTFPSADHFLTALAI SRLALIW
VLF LDSFLFIQSPLL MTRNTLR LIQTAWNISNHFSIWFATSLSIFYLFKIAIFS NYLFFY
LKRRVKRVVLVILL LSMILLFFNIFLEIKHIDVWIYGTKRNITNGLSSNSFSEFSRLILI
PSLMFTLVPFGVSLIAFLLLI FSLMKHVRKMQYYTKGCKDVRTMAHTTALQTVVAFLLLY
15 TTFFLSLVVEVSTLEMDES LMLLFAKVTIMIFPSIHSCIFILKH NKLRQDLLSVLKW LQY
WCKREKTLDS

SEQ ID NO:134

20 Mouse T2R15 nucleotide sequence

AATAATAGATTTTTTAATATTCAGAATTTTAAAGTAATGTAGTATTGTTAGCAGCATAGC
TTATAGGAAAAGTTCCAAGTAATTTTGATTTTGTAATTCTGATTCCCCCAAATCAAGTAT
CAAGTTTACCTGCACAGACAAGGGAAGAAGTGGCAAATGTGCAAATGAGAGCAACTTTA
25 TTTGACTGTCAGTACGTTGAAATTCAGTGTTTCCTTAATCAGTTATGGATTGACATTTAT
GTGCACAGAACCTGGAAGAATTTAGCCAAGCTGGAGGTAAAAATCCAAAATTCTGATGA
TAAAACCAAAAGTAAATCACAGGTAAATCTTCTTTATTTTCTTTTTTAATACTGTATAT
GGACATTTTTTAATACAGCATATTTTTTTTTTTGAAATTTAGAAAAAAACCACTAAGAAAT
ATTCACCAATGGAATAGACTTTAAAGTCACTTAGAGAATGTGTGCTGTTCTACGTAGCAT
30 ACTGACAATCATTTTCATTTTGAGTTCTTCATTGGAAATCTGGGGAATGGATTCATAGC
TCTGGTACAATGCATGGACTTACGAAAGAGAAGAACGTTCCCTTCAGCAGATCATTTCTT
CACTGCTCTGGCCATCTCCAGGCTTGCTCTGATATGGGTTTTATTTCTAGATTCATTTCT
GTTTATACAATCCCCATTACTGATGACTAGAAATACATTAAGACTGATTCAGACTGCCTG
GAATATAAGCAATCATTTTCAGTATATGGTTTGCTACCAGCCTCAGCATCTTTTATCTCTT

CAAGATAGCCATTTTTCTAACTATCTTTCTTCTACCTGAAGCGGAGAGTTAAAAGGGT
GGTTTTGGTGATACTGCTGCTATCCATGATCCTTTTGTTTTTAATATATTTTAGAAAT
CAAACATATTGATGTCTGGATCTATGGAACCAAAGAAACATAACTAATGGTTTGAGTTC
AAACAGTTTTTCAGAGTTTTCCAGGCTTATTTTAATTCCAAGTTTAATGTTTACATTAGT
5 ACCCTTTGGTGTATCCTTGATAGCTTTCCTCCTCCTAATCTTTTCCCTTATGAAACATGT
AAGGAAGATGCAGTACTACACCAAAGGATGCAAAGATGTCAGAACCATGGCCACACCAC
AGCCCTGCAGACTGTGGTTGCCTTCCTCCTATTATATACTACTTTCTTTCTGTCTCTAGT
TGTGGAAGTTTCAACACTTGAAATGGATGAAAGTCTGATGCTTCTGTTTGCAAAGTTAC
TATAATGATTTTTCTTCCATCCACTCCTGTATTTTCATTTTGAAACATAATAAGTTGAG
10 ACAGGACTTGCTTTCAGTACTGAAGTGGCTACAGTATTGGTGCAAGCGTGAGAAAACCTT
GGATTCATAGACCATTGTATGCATCACCTTGAATATTCTAGAGGGGTGTAGGTTTCATATG
AAAGTATTGAATTTTAAATTTGAGCCTTTTGTATATTTTCT

15 **SEQ ID NO:135**

Mouse T2R16 amino acid sequence

MNGVLQVTFIVILSVEFIIGIFGNGFIAVVNIKDLVKGRKISSVDQILTALAISRIALLW
LILVSWWIFVLYPGQWMTDRRVSIMHSIWTFNQSSLWFATSLSIFYFFKIANFSNPFL
20 YLKVRLKKVMIGTLIMSLILFCLNIIIMNAPENILITEYNVMSYSLILNNTQLSMLFPF
ANTMFGFIPFAVSLVTFVLLVFSLWKHQKMQHSAHGCRDASTKAHIRALQTLIASLLLY
SIFFLSHVMKVWSALLLERTLLLLITQVARTAFPSVHSWVLILGNAKMRKASLYVFLWLR
CRHKE

25

SEQ ID NO:136

Mouse T2R16 nucleotide sequence

TTTATGATGGAAAGAATAAAACCATTAGCAAGGCTTAATGGCTTGTTTGGTATTAGACCT
30 GTACATTGTTTATGGAACATGATATGGAGCTTTGTTTATTGAATATGCACAATATTTTAG
AAGCATGTTTCAAAGAATCTTAAGTAATTACAATAGAAATTGAAGCATCCAAGTGAAGAT
GAATGGTGTCTACAGGTTACATTTATAGTCATTTTGAGTGTGGAATTTATAATTGGCAT
CTTTGGCAATGGATTCATAGCGGTGGTGAACATAAAGGACTTGGTCAAGGGAAGGAAGAT
CTCTTCAGTGGATCAGATCCTCACTGCTCTGGCCATCTCCAGAATTGCACTGCTGTGGTT

AATATTAGTAAGTTGGTGGATATTTGTGCTTTACCCAGGACAATGGATGACTGATAGAAG
 AGTTAGCATAATGCACAGTATATGGACAACATTCAACCAGAGTAGTCTCTGGTTTGCTAC
 AAGTCTCAGCATCTTTTATTTTTTCAAGATAGCAAATTTTTCCAACCCTATTTTTCTTTA
 TTTAAAGGTCAGACTTAAAAAAGTCATGATAGGGACATTGATAATGTCTTTGATTCTCTT
 5 TTGTTTAAATATTATCATTATGAATGCACCTGAGAACATTTTAATCACTGAATATAATGT
 ATCTATGTCTTACAGCTTGATTTTGAATAACACACAGCTTTCTATGCTGTTTCCATTTGC
 CAACACCATGTTTGGGTTTACACCTTTTGCTGTGTCACTGGTCACTTTTGTCTTCTTGT
 TTTCTCCCTGTGGAAACATCAGAGAAAGATGCAACACAGTGCCCATGGATGCAGAGATGC
 CAGCACTAAGGCCACATCAGAGCCTTGCAGACATTGATTGCCTCCCTCCTCCTGTATTC
 10 CATTTTCTTCTGTCTCATGTTATGAAGGTTTGGAGTGCTCTGCTTCTGGAGAGGACACT
 CCTGCTTTTGATCACACAGGTTGCAAGAACAGCTTTTCCGTCAGTGCACCTCCTGGGTCCT
 GATTCTGGGCAATGCTAAGATGAGAAAGGCTTCTCTCTATGTATTCTGTGGCTGAGGTG
 CAGGCACAAAGAATGAACCCTACAGTGTACAGACCTGGGGTATATTTATGTGGATGATC
 TTACATATCTTAGAGGAAAATGGATTAAAAGAAATTCTCATATTTATAAATTTTAGGTC
 15 TGAATTACATAAAAATGTATATAATATTTTCAAAGTACAAGATAGTAGTTTATAACTTAC
 ATGATAAATACTGTCTATGCATCTTCTAGTCTTTGTAGAATATGTAAAAACATGTT

SEQ ID NO:137

20 Mouse T2R17 amino acid sequence

MKHFWKILSVISQSTLSVILIVELVIGIIGNGFMLVHCMDWVKKKKMSLVNQILTALSI
 SRIFQLCLLFISLVINFSYTDLTSSRMIVMYNAWILANHFSIWIATCLTVLYFLKIAN
 FSNSFFLYLKWRVEKVVSVTLLVSLLLLILNILLTNLETDMWTNEYQRNISCFSSSHYYA
 25 KCHRQVLRHLHIIFLSVPVLSLSTFLLLI FSLWTHHKRMQQHVQGRDARTTAHFALQT
 VIAFFLLYSIFILSVLIQIWKYELLKKNLFVVVFCEVVYIAFPTFHSYILIVGDMKLRQAC
 LPLCIIAAEIQTTLCRNFRSLKYFRLCCIF

30 **SEQ ID NO:138**

Mouse T2R17 nucleotide sequence

GAATTCTGGTCTGGCACCCCTGAGCTGTGTGAGTAGACACATTATCATGGAAAGAGATTC
 AGAATCTGTCACTGTCAAACTGCATGTTTGCTCCTCTGTTAGTGTGTTGGGGAAAGTTA

AGAAAAATACATTTTATGAGAATCAACTCAGAGGTTGTCAGAAATTGTCGAAACAGCATT
 TTAAAAATTTACATCTCAACTGGATATATGAGCAAGTCTTTATAACTGATATATAAAATG
 AAGCACTTTTGGGAAGATATTATCTGTTATCTCCAGAGCACACTTTCAGTCATTTTAATC
 GTGGAATTAGTAATTGGAATTATAGGAAATGGGTTTCATGGTCCTGGTCCACTGTATGGAC
 5 TGGGTAAAGAAAAAGAAAATGTCCCTAGTTAATCAAATTCTTACTGCTTTGTCAATCTCC
 AGAATTTTTCAGCTCTGTTTATTGTTTATAAGTTTAGTAATCAACTTTTCATATACAGAT
 TTAATAACAAGTTCAAGGATGATACAAGTCATGTACAATGCTTGGATTTTAGCCAACCAT
 TTCAGCATCTGGATTGCTACATGCCTCACTGTCCTTTATTTTCTAAAGATAGCCAATTTT
 TCTAACTCTTTTTTTCTTTATCTAAAGTGGAGAGTTGAAAAAGTAGTTTCAGTTACACTG
 10 TTGGTGTCAATTGCTCCTCCTGATTTTAAATATTTTACTAACTAACTTGGAAACCGACATG
 TGGACAAATGAATATCAAAGAAACATATCATGCAGCTTCAGTTCTCATTACTATGCAAAG
 TGTACAGGCAGGTGTTAAGGCTTCACATTATTTTCCTGTCTGTCCCCGTTGTTTTGTCC
 CTGTCAACTTTTCTCCTGCTCATCTTCTCCCTGTGGACACATCACAAGAGGATGCAGCAG
 CATGTTTCAGGGAGGCAGAGATGCCAGAACCACGGCCCACTTCAAAGCCCTACAACTGTG
 15 ATTGCATTTTTCCTACTATATTCCATTTTATTCTGTCTGTCTTAATACAAATTTGGAAA
 TATGAATTACTGAAGAAAAATCTTTTCGTTGTATTTTGTGAGGTTGTATATATAGCTTTT
 CCGACATTCCATTCATATATTCTGATTGTAGGAGACATGAAGCTGAGACAGGCCTGCCTG
 CCTCTCTGTATTATCGCAGCTGAAATTCAGACTACACTATGTAGAAATTTTAGATCACTA
 AAGTACTTTAGATTATGTTGTATATTCTAGACAAAAATTAAGTATACAAATGTCTTTTG
 20 TATTTTTCATTTTAAATATCCTTTAATTTTGACTGCATGAAATTGATTTCTGCTTGCAAT
 TATCACTGATTAAACTATTAATAATTTAACTAG

SEQ ID NO:139

25 Mouse T2R18 amino acid sequence

MVPTQVTIFSIIMYVLESLVIIIVQSCTTVAVLFWREWMHFQRLSPVETILISLGISHFCLQ
 WTSMLYNFGTYSRPVLLFWKVSVVWEFMNILTFWLTSWLAVLYCVKVSSFTHPIFLWLRM
 KILKLVLWLILGALIASCLSIIPSVVKYHIQMELVTLDNLPKNNSLILRLQQFEWYFSNP
 30 LKMIGFGIPFFVFLASIILLTVSLVQHWVQMKHYSSNSSLKAQFTVLKSLATFFFTFTS
 YFLTIVISFIGTVFDKKSFWVCEAVIYGLVCIHFTSLMMSNPALKKALKLQFWSPEPS

SEQ ID NO:140

Mouse T2R18 nucleotide sequence

GCGTGCTTCACAGAGCAGTATACTACAAAGCAAATGTCATTGCTGCCATTGTATATTTCT
CTAAAGACATTTACATTTTATCTCCCTGTCCCATTGTGTGCAGAGCCCACACTTCAATC
5 AATCAATTCCTTAATTATAAGCTATTGTTTCATTATTTTCATTTCCCTACGTTTTTTTTGCAT
TTTTACTAAAACCTCCAAAGCAGACATTTTCTAATTATAATCCTACATGTAGTTAGAATTT
TAAAAATTATATACTATTTTCTTTGCACCACTGAGTTCAGTAGGTTTTGAAGGTTTATGC
TTAACAATTGAACATTTTCATGTTAGATTATTCCTGCCTTCCTAATCTTGAATAATTAAAT
GTCCATCCAGGCTTAGAATTCACAGAGTCAACAGCTTTCACCTTGATTCTCTCACTATCT
10 ATCAATGACTAGAATCTGTCTGTCACTTTTGAAACCGCTAATTAAATAGTTGGTGCTTAT
TTAAAGGGTGCCCCATGCCAAGAGAAAATGTATTTCTTCTCTAGATGCCTTCGTCCTTTA
CAAGTTACATGCTTTACTGATGGTGAATTGGTTTTCTTCCAGTTCATCTGGGTAAAGTGA
CCTAAGAACCTAGCCATGGAAGGAGAAACAGAAGCAAATATTAACGATACAAGAACAAGT
TCCAGAACATTGGAAAGTACTTAGTAAAGGCATTGGAATTAGCAAAAAGATAGTAGCGAA
15 GCAAAAATACTTCATCTCCATTGGGAGGTCAAGAAAGACTATGCAGTGTTTTTGATGCA
ACTTGTCATCTCTGAGTTAGACGATTCAGCACACACTTTTGAGATTGAACTTCAACAGGT
GGAGCCAGCAGACCTGAGCTTTAGGAATGATGGTGGAATTTCCAAGCAAAGACTTCCGTT
ACCTTTTTTGATGTCCCCTAACAAATTCGGTTGCAATGCTCACACCGCCCACTGTTGAAAT
GCTTGGGAAAAGGGATTCTGAGACTGGCATTAGTATGTCATTTGACAGAATGGAAACATT
20 GCCCAGGGCATTAAATGCACAGTAAAGGATTCACCTTTTCTAAGTGCTCAAATTTTAAATT
TGnATATTTTTTAGAAGACATTATTTAAAAGAAAGGTGGAGAGGATATCCAAACAGCACCT
TGAGCAGATAAAGAGGTGAAGAAGAAAAACAACATGCGTACATGATGGATTTCTCTTTA
TGAAATGATCAAATGATCTTAGGATCAAGAATCCACACCTGAATGAGATTTGCTTGAT
CCCTGTGTGAATTTGACCTAACAAAGCAAAGCACAGACAAATGCTGTAGATAGGGAAATGT
25 CTATGTCAAATGTGTGTAAGGAGGATTTGCATCCACAAAGAAGTGCCCTCTTATACTGAG
AGTGCTAAGAACACATGTCCGTTTCATATTCGGAAAGTGGTATAGAGCTGTTGAGTCTTT
GGCTAGGAAGAGACTTCAGAGTGGAAGC**ATGGTGCCAACGCAAGTCACCATCTTCTCCAT**
CATCATGTATGTGCTTGAGTCCTTAGTAATAATTGTGCAAAGTTGCACAACGGTTGCAGT
GCTATTCAGAGAGTGGATGCACTTTCAAAGACTGTCACCGGTGGAGACGATTCTCATCAG
30 **CCTGGGCATCTCACATTTCTGTCTACAGTGGACATCAATGCTATACAACCTTTGGTACTTA**
TTCTAGGCCTGTCCTTTTATTTTGGAAAGGTATCAGTCGTCTGGGAGTTCATGAACATTTT
GACATTCTGGTTAACAGTTGGCTTGCTGTCTCTACTGTGTCAAGGTCTCTTCCCTTAC
TCACCCCATCTTCCCTCTGGCTGAGGATGAAAATCTTGAAACTGGTTCTCTGGTTGATACT
GGGTGCTCTGATAGCTTCTTGTTTGTCAATCATCCCTTCTGTTGTTAAATATCACATCCA

GATGGAATTAGTCACCCTAGATAATTTACCCAAGAACAATTCTTTGATTCTAAGACTACA
 ACAGTTTGAATGGTATTTTTCTAATCCTTTAAAAATGATTGGCTTTGGTATTCCTTTCTT
 CGTGTTCTGGCTTCTATCATCTTACTCACAGTCTCATTGGTCCAACACTGGGTGCAGAT
 GAAACACTACAGCAGCAGCAACTCCAGCCTGAAAGCTCAGTTCAGTGTCTGAAGTCTCT
 5 TGCTACCTTCTTCACCTTCTTCACATCCTATTTTCTGACTATAGTCATCTCCTTTATTGG
 CACTGTGTTTGATAAGAAATCTTGGTTCTGGGTCTGCGAAGCTGTCATCTATGGTTTAGT
 CTGTATTCACCTTCACTTCACTGATGATGAGCAACCCTGCATTGAAAAGGCACTGAAGCT
 GCAGTTCTGGAGCCCAGAGCCTTCTGAGGAGGAGGAAACACAGTTAAGCCTCTAGGGTAAG
 GAGACTTTGCATTGGCACAGTCCCTATAGTGTAATGCAAACCTTGAACACAACTTCATCC
 10 CTTTTACATCCACAAATGGCTGCATCTATACATCATCACCAGTCTTCCCTGTATTCTGA
 CCCATTCTCTTCCCTGTCTATCCATAGTCCCCAGGTTGGTTTTGATTTTTCTCATGATCA
 CACCAACTCTGCTTAGCTTTTGCCACCACTGTAATAGTAAACATGGGGTGTTCTATATAT
 TACAGTCAAATCATTCTCACATTGTTGATTGCCTCACAAATTCATATAAATCCCCCTTC
 CTGTCAGGAATTTATTGTCTGCTCACTTAATGCTCACCATATATTAAAGCCATTAATTCC
 15 CCCTTCCTACCTTGAGTTTAAGAAGGAAAATGTCTTACCATTGCCCACAACCTATTCTGC
 TGCTTCTAGACTTTTATGCAAGTGATTTATACACACACACACACACACACACATAC
 AAACAAC

20 **SEQ ID NO:141**

Mouse T2R19 amino acid sequence

MMEGHMLFLLLVVVVQFLTGVLANGLIVVNAIDLIMWKKMAPLDLLLFLCLATSRILQL
 CILFAQLGLSCLVRHTLFADNVTFVYIINELSLWFATWLGVFYCAKIATIPHPLFLWLKM
 25 RISRLVPWLILASVVYVTVTTFIHSRETSELPKQIFISFFSKNTTRVRPAHATLLSVFVF
 GLTLPFLIFTVAVLLLLSSLWNHSRQMRMTVGTREPSRHALVSAMLSILSFLILYLSDM
 VAVLICTQGLHFGSRTFAFCLLVIGMYPSSLHSIVLILGNPKLKRNAKTFIVHCKCCHCAR
 AWVTSRNPRLSDLPVPATHHSANKTSCSEACIMPS

30

SEQ ID NO:142

Mouse T2R19 nucleotide sequence

MNLVEWIVTIIIMMTEFLLGNCANVFITIVNFIDCVKRRKISSADRIITAIAIFRIGLLWA
MLTNWHSVFTPDNDNLQMRVFGGITWAITNHFTTWLGTILSMFYLFKIANFSNSLFLHL
KRKLDNVLLVIFLGSLLFLVAYLGMVNIKKIAWMSIHEGNVTTKSKLKHVTSITNMLLES
LINIVPFGISLNCVLLLIYSLSKHLKNMKFYGKGCQDQSTMVHIKALQTVVSFLLLYATY
5 SSCVVISGWSLQNPVFLFCVTIGSFYPAGHSCILIWGNQKLKQVFLLLLRQMRC

SEQ ID NO:144

Mouse T2R20 nucleotide sequence

10 CTAGATGGGCTGTTTCATATAATGACTGGAACCTCCCTACATGCTCCACGTCTTGAGTTCT
AAAATTTCACTAACAAATTTTTGACTGCCATAAATAATGAAGGTTTAAAGAAAGAACAAC
ATTTGAAGCAATGGACCAGAATTCCTCTTTATTTGACTCTTAGCAAATTGGAATGCAGCA
TCCTTTCAAGAGCAGCACTGAAATATAACAGTCAATGGCAGAGAGTAAAAAGTATGCAA
15 TTGGAGACATTATGGTAATATAAATTTCCATTAAAAATGAGACTGCATTACCTATTACA
ACACATTGCTATTCTGCTCAACACAGAGTTAAAAAGAAACAAGAACTCTTGATACATTC
AGTTAGTCACAAGTATAATTATGTTACATATTTTAAAAAATGAATCATGATCTGTGAA
TTGAGCCTGGCTTTTTTTGTCTCTCTCTTTTATTCTTTTCCTTTAGACAGACACA**ATGA**
ATTTGGTAGAATGGATTGTTACCATCATAATGATGACAGAATTTCTCTTAGGAACTGTG
20 **CCAATGTCTTCATAACCATAGTGAACCTTCATCGACTGTGTGAAGAGAAGAAAGATCTCCT**
CAGCTGATCGAATTATACTGCTATTGCCATCTTCAGAATTGGTTTGTGTGGGCAATGT
TAACGAACTGGCATTACATGTGTTTACTCCAGACACAGACAATTTACAAATGAGAGTTT
TCGGTGGAAATTACCTGGGCTATAACCAACCATTTTACCACCTGGCTGGGGACCATACTGA
GCATGTTTTATTTATTCAAGATAGCCAATTTTCCAACAGTCTATTTCTTCATCTAAAAA
25 **GAAAACTTGACAATGTTCTACTTGTGATTTTCTGGGATCGTCTCTGTTTTTGGTTGCAT**
ATCTTGGGATGGTGAACATCAAGAAGATTGCTTGGATGAGTATTCATGAAGGAAATGTGA
CCACAAAGAGCAAACCTGAAGCATGTAACAAGCATCACAAATATGCTTCTCTTCAGCCTGA
TAAACATTGTACCATTGGTATATCACTGAACTGTGTTCTGCTCTTAATCTATTCCCTGA
GTAAACATCTCAAGAATATGAAATTCTATGGCAAAGGATGTCAAGATCAGAGCACCATGG
30 **TCCACATAAAGGCCTTGCAAACCTGTGGTCTCTTTTCTCTTGTTATATGCCACATACTCTT**
CCTGTGTCATTATATCAGGTTGGAGTTTGCAAAATGCACCAGTCTTCCTGTTTTGTGTGA
CAATTGGATCCTTCTACCCAGCAGGTCATTCTTGTATCTTGATTTGGGGAAACCAGAAAC
TTAAACAGGTCTTTCTGTTGTTGCTGAGGCAGATGAGATGCTGACTGAAAAAATGAAAGT
CCCCCTGTCTCTAG

SEQ ID NO:145

Mouse T2R21 amino acid sequence

5

MGSNVYGILTMVMIAEFVFGNMSNGFIVLINCIDWVRKGTLSIGWILLFLAISRMVLIW
EMLITWIKYMKYSFSFVTGTELRGIMFTWVISNHFSLWLATILSIFYLLKIASFSKPVFL
YLKWREKKVLLIVLLGNLIFLMLNILQINKHIEHWMYQYERNITWSSRVSDFAGFSNLVL
LEMIVFSVTPFTVALVSFILLIFSLWKHLQKMHLNSRGERDPSTKAHVNALRIMVSFLLL
10 YATYFISFFLSLIPMAHKTRLGLMFSITVGLFYPPSSHFILILGHSNLRQASLWVMTYLK
CGQKH

SEQ ID NO:146

15 Mouse T2R21 nucleotide sequence

CTCTTTTGAAGACAATAGTTGTTCTACTAGCTATTGATAGCATGTTTACATTTGTCATTT
TCAAGTATGTTTCAGAAACAAAGCTACATATTGTGGGGAGTATATAAAATATGAAAGCATG
CCATTCCCAGGCATCCAAGGATCCCTGTGTATTAAAAGGCAACAAAGCAGAACCAAATGT
20 TCTGTTTTGGACATGAGCTTCTTCCAATTCAACTGCTGAAAAATTTGGATAACTACATAT
AAAATAAGAACACAGAGTGTACAGAGCAGTCTCTGCTCTCCAATTCACCAGGATTAAT
ATTGACAGACCCAAAAGATGTCATTTAGGTAAATTTTGGATGAATCATATTGTTGTCACC
TTTGTGCTCTAGAACATAAGCTGATAGAATCAAATTTTCTTTAGCAGAGACAATGCAAAT
TGATATAACAGTGAAAGAGAATATATCTTTATTTGCATGTTAGCAAATGACAGCTGGATG
25 CACTTCATGATTTTCTGCAATCTAGTTCAGTCTTTAGAAGGATATATATATATATATATA
TATATATATATATATATATATATATATATATATAAACCTTAGTCTTGAAAGATATCAGAA
AGAAGGATTTCAACAAGATGTACAGAGCCATTAGCAAAATTTTAATATACTCATCGACAT
TAGGTCAGTCACTACATAAGAAGGACTTGAATGAAAGCTTATCTTAGTTTTTGAGACTAC
AGGGACATTTACCTTGCCAAATGAGAAGCAGTGAGTCTTCTTTGTCTGGACATGGGAAG
30 CAATGTGTATGGTATCTTAACTATGGTTATGATTGCAGAGTTTGTATTTGGAAATATGAG
CAATGGATTCATAGTGCTGATAAACTGCATTGATTGGGTGAGGAAAGGAACTCTTTCCTTC
CATTGGTTGGATCCTGCTTTTCTTGGCCATTTCAAGAATGGTGTTGATATGGGAAATGTT
AATAACATGGATAAAATATATGAAGTATTCATTTTCATTTGTGACTGGAACAGAATTACG
GGGTATCATGTTTACCTGGGTAATTTCCAATCACTTCAGTCTCTGGCTTGCCACTATTCT

CAGCATCTTTTATTTGCTCAAAATAGCCAGTTTCTCCAAACCGGTTTTTCTCTATTTGAA
 GTGGAGAGAGAAGAAAGTGCTTCTGATTGTCCTTCTGGGAAATTTGATCTTCTTGATGCT
 CAACATATTACAAATAAACAAACATATAGAACACTGGATGTATCAATATGAGAGAAATAT
 AACTTGGAGTTCTAGAGTGAGTGACTTTGCAGGGTTTTCAAATCTGGTCTTATTGGAGAT
 5 GATTGTGTTCTCTGTAAACACCATTACAGTGGCCCTGGTCTCCTTCATCCTGTTAATCTT
 CTCCTTGTGGAAACATCTACAGAAAATGCATCTCAATTCTAGAGGGGAACGAGACCCAG
 CACTAAAGCCCATGTGAATGCCTTGAGAATTATGGTCTCCTTCCTCTTACTCTATGCCAC
 TTACTTCATATCTTTTTTTCTATCATTGATCCCATGGCACATAAAACACGACTGGGTCT
 TATGTTTAGCATAACTGTTGGGCTTTTCTACCCTTCAAGCCACTCATTTATCTTAATTTT
 10 GGGACATTCTAATTTAAGGCAAGCCAGTCTTTGGGTGATGACATATCTTAAATGTGGGCA
 AAAGCATTAGAATTTCACTATTCCATAAGGCAGCCAAACCACGTGCTACTAGGTATATGA
 TACTACTCAGTGGTAAAGCCCTAGGCCAAACATTAACCTTAGAAAATATATAATTTTGTGA
 CTCTTCTGTATTTGATAAATCACTCACATATTTAGAAGAATGCTACAGTAGTGTGATCTT
 GTACATGATTGTAACAATTCAATTTTATTAATATAGTTCAGGCATGATAACATACCCCTG
 15 ATAAGTAAAAGTAAGTAGGATGCTACATATATATTTAGATCTAGACTTAGGGGCAAAGA
 GAGACCCAGCTGATAGCTGTGCAATAAAGATTTTAATTTTCATCCTGTTGTGAGTTATCT
 GAAATCTATGTCACTGAAGGCATAAGCAAGATTTTCACACACTGAAACAATCTCTTATGC
 TTTCTTATATTGTTTTTAAAAGTAAATTAGAAAATTTAAATAAACTTAATGGCAATTGAAA
 TTACAAAAGCTAAACACATGTGGTTATTAGAAATTAGACTGTATGTAGGTCCTAGGGGAT
 20 GGCTTAGTAAAGTGCTTTGTTGCAAGCTTCAGGATATGATTCTAAATCCCTAGATTCAAT
 TAAAAACCTGGCATAAATAGCCAATGTAAAATTTGTCTGTAAAATGTAACCAGTGCTAAG
 AGTACCAAGACAACAAAATGTTTACTTTTAAAACCATTTATTGATATTCTTTTAAAAATA
 GGTATGTATTTTACTATTTAAATAAGATTTTGTCAAAGCTAGTCTTGACACCTTAGGTA
 AACATAGGAAGGCAACAAGTTTGAAGTCAGCTACTGGGGACAGTGCTGCTAGCAGCTGAC
 25 AGAGGCCACTGCTGACTACAGCAGATCATTTACAGGTTCAGCACTAG

SEQ ID NO:147

Mouse T2R22 amino acid sequence

30 MSSLLEIFFVVIISVVEFIIIGTLGNGFIVLINSTSWFKNQKISVIDFILTWLAISRMCVLW
 TTIAGASLRKFYKTLSSKNFKFCFDIWTGSNYLCIACTTCISVFYLFKIANFSNSIFF
 WIKQRIHAVLLAIVLGTLMYFILFLIFMKMIANNFIYKWKLEQNTTFPVLDTLSGFLVY
 HSLYNGILIFFFIVSLTSFLLLIIFSLWSHLRRMKLQGIHTKDISTEAHIKAMKTMMSFLL

FFIIYYISNIMLIVASSILDNVVAQIFSYNLIFLYLSVHPFLLVLWNSKWKWTFQHVLRK
LVCHCGGYS

5 **SEQ ID NO:148**

Mouse T2R22 nucleotide sequence

AAATGAATAATTTTCATGCAAAGGATACCATTAGAATATGATCACTATTTAAATTTTAGCA
AATACATATTTCAAATACCAGCACAAATGTTTCAAATTTAAAATATAAACATTATAAAACCC
10 AGCAGAGAACAAAATGATAGCCTTGATAATTGTTGGTTTGCTCAAGAAAAATGGGTGTAT
ACTTTAACATTTAATTGGGAACCTCAGTTGAGAGCATACTTTAGGGTTTTACAGAGGTAT
TCATTGCCCATTTAAGATTTGGATTACACATCTACATCAATGTGGCTGTAATCCATTTT
CCCATGATGAAATAAGGTAGAGACTGCCTATTAAACGACATGTCGAGCCTACTGGAGATT
TTCTTTGTGATCATTTTCGGTTGTAGAATTCATAATAGGAACTTTGGGAAATGGATTTATT
15 GTCCTGATAAACAGTACTTCTTGGTTCAAGAATCAGAAAATCTCTGTAATTGATTTCAAT
CTTACTTGGTTGGCCATCTCCAGAATGTGTGTTCTATGGACAACAATTGCTGGTGCCTCT
CTCAGGAAATTCTACAAGACGTTAAGTTACTCTAAGAATTTCAAATTTTGTTTTGACATT
ATCTGGACAGGATCCAACATTTTATGCATAGCCTGTACAACGTGCATCAGTGTCTTCTAC
TTGTTCAAGATTGCCAACTTTTCTAATTCATTTTCTTCTGGATTAAACAGAGAATTCAT
20 GCAGTACTTCTGGCTATTGTCCTAGGCACACTCATGTATTTCAATTTTATTTCTCATTTTT
ATGAAAATGATAGCTAATAATTTTATCTACAAATGGACAAAATTGGAACAAAACACAACA
TTCCCTGTTTTAGATACTCTAAGTGGTTTCTTAGTCTACCATAGCCTCTACAATGGGATT
CTCATTTTCTTTTTTATAGTGTCTCTGACCTCATTTCTTCTTTTAATCTTCTCTTTATGG
AGCCACCTTAGGAGGATGAAACTACAGGGCATAACCAAGACATAAGCACAGAAGCA
25 CACATAAAAGCTATGAAACTATGATGTCATTCCTTTTGTTCCTTCATCATATATTATATT
AGCAACATTATGCTTATTGTGGCAAGCTCCATTCTTGACAATGTGGTTGCACAAATTTTC
TCTTATAACCTAATATTTCTGTATTTATCTGTTTCATCCTTTTCTTCTGGTTTTATGGAAC
AGCAAATTGAAATGGACATTCCAGCATGTATTGAGAAAGCTGGTGTGTCAATTGTGGAGGT
TATTCTTGATTTTCAGTAAATACACTCAATATAACTGATGGATTTCTAAGGTAAGAAAAAT
30 GGAACAAGGAATAAAGAGGAGAAATATATTCCTTTTCAGATCATCTGCTCTGTCATTCTG
TCCTTAGCATGCTATTAAGAATTGTTGACTAAATCCAGTCATTTTAAACATGAGGAAAGG
ATGTTTCAATCCAACCTTAGAGAGGGTACAAAATAGTCCTAGGAGGCAG

SEQ ID NO:149

Mouse T2R23 amino acid sequence

MFSQKINYSHLFTFSITLYVEIVTGILGHGFIALVNIMDWVKRRRISSVDQILTALALTR
5 FIYVLSMLICILLFMLCPHLPRRSEMLSAMGIFWVVNSHFISIWLTTCLGVFYFLKIANFS
NSFFLYLKWRVKVILIIILASLIFLTLHILSLGIYDQFSIAAYVGNMSYSLTDLTQFSS
TFLFSNSSNVFLITNSSHVFLPINSFLMLIPFTVSLVAFMLLIFSLWKHHKKMQVNAKQP
RDVSTMAHIKALQTVFSFLLLYAIYLLFLIIGILNLGLMEKIVILIFDHISGAVFPISHS
FVLILGNSKLRQASLSVLPLRCQSKDMDTMGL

10

SEQ ID NO:150

Mouse T2R23 nucleotide sequence

15 AATTTTCAGCAACCAATATGTAGACTGCTTAAATGCATCAGAAACATTATAAATTGAAGC
ATGTTTTTCACAGAAAATAAACTACAGCCATTTGTTACTTTTTCAATCACCTTGTATGTG
GAAATAGTAACGGGAATCTTAGGACATGGATTCATAGCATTAGTGAACATCATGGACTGG
GTCAAAGAAGAAGGATCTCTTCAGTGGATCAGATTCTCACTGCTTTGGCCCTTACCAGA
TTCATTTATGTCTTGTCTATGCTGATTTGCATATTGTTATTCATGCTGTGCCACATTTG
20 CCTAGGAGATCAGAAATGCTTTCAGCAATGGGTATTTTCTGGGTAGTCAACAGCCATTTT
AGCATCTGGCTTACTACATGCCTCGGTGTCTTTTATTTTCTCAAGATAGCCAATTTTCT
AACTCTTTTTTCTTTATCTAAAGTGGAGAGTTAAAAAGTGATTTTAATAATAATCCTG
GCATCACTGATTTTCTTGACTTTACACATTTTATCTTTAGGGATATATGATCAGTTCTCA
ATTGCTGCTTATGTAGGAAATATGTCTTATAGTTTGACAGATTTAACACAATTTTCCAGT
25 ACTTTCTTATTCTCCAATCATCCAATGTTTTCTTAATCACCAACTCATCCCATGTTTTT
TTACCCATCAACTCCCTGTTTCATGCTCATAACCTTCACAGTGTCCCTGGTAGCCTTTCTC
ATGCTCATCTTCTCACTGTGGAAGCATCACAAAAGATGCAGGTCAATGCCAAACAACCT
AGAGATGTCAGTACTATGGCCACATTAAAGCCTTGCAAAGTGTGTTCTCCTTCCTGCTG
CTGTATGCCATATACTTACTTTTCTTATCATAGGAATTTTGAACCTTGGATTGATGGAG
30 AAAATAGTGATACTGATATTTGACCACATTTCTGGAGCAGTTTTTCTTATAAGCCACTCA
TTTGTAAGTCTGATTCTGGGAAACAGTAAGCTGAGACAAGCCAGTCTTTCTGTGTTGCCTTGT
CTAAGGTGCCAGTCCAAAGATATGGACACCATGGGTCTCTAGTAAATTCCAGAGTACATT
TTGTAAAAATCTTGAGGATGATCAGTTCATAGAAAAAGTTACCTTATGGGGGAAAATAA
AAAGTGGGGCTTCAATCCTGGGAGTAATAATACACAGGAGGGTAGGACAGCATGAAGGAG

ACTAGCACTATATAAGTGGTCTCATACAGGATATGGGAAAGGAAAGATTTATGCAATAAA
GAGGGAGATCATATTGGAGGATGAGGAGGCATTACATATGTAAAATGACTATAAGAATGG
AATCATGCTAATCTAAAAAATCTGTAATGCATTTTCATTCAGACTATATACATATATGCC
TATATATGGATATATGGGGATATATATTCTATACATATTTTAAAAGAACCTTTCTTATAT
5 AG

SEQ ID NO:151

Mouse T2R24 amino acid sequence

10

MVPVLHSLSTIIILIAEFVWGNLSNGLIVLKNCIDWINKKELSTVDQILIVLAISRISLIW
ETLIIWVKDQLISSITIEELKIIIVFSFILSSHFSWLATALSIFYLFRIIPNCYWQIFLYL
KWRIKQLIVHMLLGSLVFLVANMIQITITITLEERFYQYGGNTSVNSMETEFSILIELMLFN
MTMFSIIPFSLALISFLLLIIFSLWKHLQKMPLNSRGDRDPSATAHRNALRILVSFLLLYT
15 IYFLSLLISWVAQKNQSELVHIIICMITSLVYPSFHSYILILGNYKLKQTSWVMRQLGCR
MKRQNTPTT

SEQ ID NO:152

20 Mouse T2R24 nucleotide sequence

CAAAGAGGAGAAATATTTAGCTACACAGTGTACCACATACAAGCCGTTCAATCAGTATAA
GGGGAGCAGTCATATAGAATTTGGGCTTTCTTTCTTTTAATATGGTACCTGTTCTGCACA
GTCTCTCCACCATCATACTAATTGCAGAGTTTGTTTGGGGAAATTTGAGCAATGGTTTGA
25 TAGTGTTGAAGAACTGCATTGACTGGATCAATAAAAAAGAGCTCTCCACAGTTGATCAAA
TACTCATTGTCTTGGAATTTCAAGAATTAGTCTCATCTGGGAAACACTAATTATATGGG
TTAAAGATCAACTAATTTTCATCTATTACTATTGAAGAATTAAAAATAATTGTGTTTCAGCT
TTATACTATCTAGCCACTTCAGTCTCTGGCTTGCTACAGCTCTCAGCATCTTCTATTTAT
TCAGAATACCTAATTGCTACTGGCAGATCTTTCTCTACTTGAAATGGAGAATAAAGCAAC
30 TGATTGTCCACATGCTTCTGGGAAGCTTGGTGTTCTTGGTTGCAAATATGATACAGATAA
CCATCACTCTTGAAGAGAGGTTCTATCAATATGGAGGAAATACAAGTGTAATTCCATGG
AGACTGAGTTCTCAATTTTGATAGAGCTGATGTTATTTAACATGACTATGTTCTCCATTA
TACCATTTTCATTGGCCTTAATTTCTTTCTTCTGCTAATCTTCTCTTTATGGAAACATC
TCCAGAAGATGCCACTCAATTCTAGAGGAGATAGAGACCCTAGTGCTACGGCCACAGAA

ATGCCTTGAGAATTTTGGTCTCCTTCCTCTTGCTCTATACTATATATTTCTGTCTCTTC
 TTATATCATGGGTTGCTCAGAAGAATCAAAGTGAAGTGGTTCACATTATTTGTATGATAA
 CTTCACTCGTGTATCCTTCATTCCACTCATATATCCTGATTCTGGGAAATTATAAATTAA
 AGCAGACCTCTCTTTGGGTAATGAGGCAGCTGGGATGTAGGATGAAAAGACAGAATACAC
 5 **CAACTACATA**AGGCAGCCAAACAGTCTATTGGGTTTTAGATAACAAATCTAAATCTATGA
 GGAAGTAGTTCAATAACATTTTTCCCTTGACATGGAGTAGCAGGGTTTTTTTTTATTAG
 ATATTTTCTTTACTTACATTTCAAATGCTATCCCGAAAATTCCTGTACCCTCTCCCTGT
 CCTGTTCCCTACCCACCCACTCCCCTTCTTGGCCCTGGCATTCCCCTGGAGTATCAGT
 TTTTATTAGTCAAACATCTCACTGACTAAGGGTCATAAAACAAGTTATTTTAACACTA
 10 ATTTCAATTAAATCAAAGGTAAAGTGTGAGCACATGCCTTTAATCACACAATTCATCAA
 ATTCAGCACTCAGGAGAGGGTGATCTCTGTGAATTCCAGCACACTGGCGGCCGTTACTAG
 TGGATCCGAGCTCGGTACCAAGCTT

15 **SEQ ID NO:153**

Mouse T2R25 amino acid sequence

MMGIAIDILWAAIIIVQFIIGNIANGFIALVNIIDWVKRRKISLMDKIITALAISRIYLL
 WSTFLITLTSSLDPIKMAVKIIRISNNTWIIANHFESIWFATCLSIFYFLKIANFESNYIF
 20 LYLRWRFKKVVSVTLLISLIFLLLNILLNMHIDIWSDKSKRNLSFSVRSNNCTQFPRLV
 LLINTMFTSIPFTVSLLAFLLLIFSLWRHLKTMQYYAKGSEDTTAAHIKALHMOVFAFL
 FYTVFFLSLAIQYWTSGSQENNNLFYATIVITFPSVHSCILILRNSQLRQASLLVLWLL
 CKSKDVRMLVP

25

SEQ ID NO:154

Mouse T2R25 nucleotide sequence

AAAACTATTCTGAATTGAACACAGTAACCAATTCTTCAGCGGACTTACACAAATCAAGCTA
 30 TTATCTTATGGATGATGGGTATTGCCATAGATATCTTATGGGCAGCTATTATCATTGTGC
AATTCATAATTGGGAATATTGCAAATGGATTCATAGCATTGGTGAACATCATAGACTGGG
TGAAGAGAAGAAAAATCTCTTTAATGGATAAGATCATTACTGCTTTGGCAATCTCTAGGA
TTTATCTGCTGTGGTCTACATTCTTAATTACACTAACATCTTCACTGGATCCAGATATTA
AAATGGCTGTGAAAATCATTAGAATAAGCAATAACACCTGGATTATTGCAAATCATTTCA

GCATTTGGTTTGCTACATGTCTCAGCATCTTTTATTTTCTCAAGATAGCCAATTTTTCTA
 ACTATATTTTTCTCTACTTAAGGTGGAGATTTAAGAAGGTGGTTTCAGTGACATTGCTAA
 TCTCTCTTATCTTCCTGCTTTTAAATATTTTACTGATGAACATGCATATTGATATCTGGA
 GTGATAAGTCCAAAAGAAACCTTTCTTTTAGTGTGAGATCAAATAATTGCACTCAGTTTC
 5 CCAGACTTGTCCTTTTAATCAACACAATGTTACATCAATCCCCTTCACTGTGTCCCTGT
 TGGCTTTTCTGCTTCTCATCTTCTCCCTGTGGAGACACCTGAAAACCATGCAATACTATG
 CTAAAGGCTCCGAAGACACCACCACAGCTGCACATATAAAGGCCTTGACATGGTAGTGG
 CCTTCTCCTGTTCTACACAGTTTCTTTTTGTCTCTTGCCATACAATATTGGACCTCTG
 GGTCTCAAGAGAATAACAACCTGTTTTATGCCACAATTGTAATTACTTCCCTTCAGTCC
 10 ATTCATGTATCCTGATTCTGAGAAACAGCCAGCTGAGGCAGGCATCTCTGTTGGTGCTGT
 GGTGGCTGCTGTGCAAGTCCAAAGATGTACGGATGTTGGTTCCTGAAATACTCTGTCAA
 TGCTCTTTAGTAGTGAAGAAGAAAATAGCTTAGTTAAGGAAATTCTTGTTTCATTACCGAA
 GTATACTTTCAAGTTTATGTATC

15

SEQ ID NO:155

Mouse T2R26 amino acid sequence

MLPTLSVFFMLTFVLLCFLGILANGFIVLMLSREWLLRGRLLPSDMILFSLGTSRFFQQC
 20 VGLVNSFYFLHLVEYSGSLARQLISLHWDFLNSATFWFCTWLSVLFCIKIANFSHPAFL
 WLKWRFPALVPWFLLGSILVSVIVTLLFFWGNHTIYQAFLLRKFTGNTTFKEWNRRL
 YFMPLKVVTMSIPCSLFLVSILLISSLRRLHSLRMQHNTHSLQDPNVQAHSRALKSLISF
 LVLYAVSFVSMIIDATVFISSDNVWYWPWQIILYFCMSVHPFILITNNLRFRTFRQLLL
 LARGFWVA

25

SEQ ID NO:156

Mouse T2R26 nucleotide sequence

GAATTCTAGACAAGGAAAGACACACACTAAATGACTTTACTTGTGGGACCTAAAATAACC
 AAAATAAGTCAAAATCACAGTGATGTTACTAGGGATCTAGGATAAGGGAATGAAGAGAAA
 GATGTTGGTCATAGAGTACAAAAATTCAGCTAAGAACTCAGTCCTGGAGGCTGAATGTAT
 AGCTGTGTGACAGACAGCAGCTAGCCATAACCAGAGTATACACTGCCTCTTGCTGAAAGA
 GTAGATCTTATGTGTCCTTGTCACACATAAAAGTAATTGAAAAAGTAACTCTCTGAGATG

AGAAGGCTTGGTCTCTTTATCTAGAGCCTTTGAAGAGACTCAGGTGAGGGTAACTTCACT
 TGGAAGTGAGCTCATCTACGTGGAAATGTCTTTGTAGGCAGGCATGGGGTCATACTGTGA
 GGTTCCTCATTGGGAAAGAGGAGAAGAAAATACAGAGTGTCCCTTACCTTAGGATAT
 TATGAAAGTGGAATTCGGAATCCTGGACCAGTATTGATCTAAGTGCAAAGTACAATATG
 5 TCCTGTTCCCTTTCATGTCTGTTTTCCCTTTTGTACTGATTCACTCTCTAGGGAATAGTCT
 TGATCAACTGAATCATCTCATCTGGCTGGCCACTGGGGAGGTAAAAGAACTTTGTGTCAC
 TGCTGCATTGGGATATACATGGGTGGGAAGCAAGTGTCCCTGAGGCAGAGTAGCACTCAG
 TATGAGAACCTCAAAGAGCAGGTGGCTGTGCATGCAGGGGCTGGGGCAAGGAGTCCTGAT
 CACTCTTCACTGTATGGGGATTATTTGTCTCTTGCCAAAATTTGGAGACTTTGGCTTTAG
 10 TTTTGTGAAGATGACTGGAAAAATTCTTAATGCTACCCTGTATCATTTCTCAATAATATT
 TTCCTTTTCCTGCCTTTAATTTTCTCCTATCTGCAGCGCCCCTTGCTTGTTATCCGTAAA
 TAAATAAATAAATAAATAAATAAGCCCAATCCTCATTTTCCTGTCTTTGGGAACCCTTTT
 ACTTCCCCAGGTATACGCTACAAAGCCACTTCTGCATTGAATAAACATTATCTTTCATTC
 AGAAAAAGACTTAAGAATCTCACCTTTACAAAAAAAAAAAAAAAAAGAATCTCACTTATTT
 15 TATATTCAAATTCATTTTTTAAAAAGAAAAGCACAGCATTAATTTTTCTAAATACTGTTT
 ATAAAAATAACTTGCTCTAAGAATTATACAAATGTTTTGAAAGGTAACCTTTGGAAAAAAA
 GTGTGATTAGACATGGATGTTTGTAAGACAGAACAAAGAGCTCTTGGAAGTCCATGGCAG
 CTCATTGGTCTTGCCTTCAGTAGAGCCTGTCTGAATCCTGTAACCTCTTATGCCCTTTTG
 TAGCTTTTCTGCAGATC

20

SEQ ID NO:157

Mouse T2R27 nucleotide sequence

25 GAATTCGCCCTTGCGGGATCCGGGAACGGATTCATAGCACTGGTAACTTCATGGGCTGG
 ATGAAGAATAGGAAGATTGCCTCCATTGATTTAATCCTCACAAGTCTGGCCATATCCAGA
 ATTTGTCTATTGTGCGTAATACTATTAGATTGTTTTATATTGGTGCTATATCCAGATGTC
 TATGCCACTGGTAAAGAAATGAGAATCATTGACTTCTTCTGGACACTAACCAATCACTTA
 AGTATCTGGTTTGCAACCTGCCTCAGCATTTACTATTTCTTCAAGATAGGTAATTTCTTT
 30 CACCCACTTTTCCTATGCCTCAAGTCTAGACGCCAAGGGC

SEQ ID NO:158

Mouse T2R28 amino acid sequence

GREWLRYGRLPLDMILISLGASRFCLQLVGTVHNFFYSAQKVEYSGGLGRQFFHLHWHF
LNSATFWFCSWLSVLFCVKIAN

5

SEQ ID NO:159

Mouse T2R28 nucleotide sequence

GAATTCGCCCTTGCGGGATCCGGGAACGGGTTTATTGTGCTGGTGCTGGGCAGGGAGTGG
10 CTGCGATATGGCAGGTTGCTGCCCTTGGATATGATCCTCATTAGCTTGGGTGCCTCCCGC
TTCTGCCTGCAGTTGGTTGGGACGGTGCACAACCTTCTACTACTCTGCCCAGAAGGTCGAG
TACTCTGGGGGTCTCGGCCGACAGTTCTTCCATCTACACTGGCACTTCCTGAACTCAGCC
ACCTTCTGGTTTTGCAGCTGGCTCAGTGTCTGTCTGTGTGAAGATTGCTAACATCACA
CACTCCACCTTCCTGTGTCTCAAGTCTAGACGCCAAGGGCG

15

SEQ ID NO:160

Mouse T2R29 amino acid sequence

MDGIVQNMFTFIVIVEIIIGWIGNGFIALVNCIHWHYKRRKISALNQILTALAFSRIYLLL
20 TVFTVIAVSTLYTHVLVTRRVVKLINFHLLFSNHFSMWLAACLGLYYFLKIAHFPNSIFV
YLMRINQVVSGTLLMSLGLLFLNTLLINSYIDTKIDDYREHLLYDFTSNNTASFYRVIL
VINNCIFTSIPFTLSQSTFLLLI FSLWRHYKKMQQHAQRCDVLADAHIRVLQTMVTYVL
LCAIFFLSLSMQILRSELLKNILYVRFCEIVA AVFPSGHSCVLICRDTNLRGTFLSVLSW
25 LKQRFTSWIPNINCRSSCIF

SEQ ID NO:161

Mouse T2R29 nucleotide sequence

30

AGCTTGATATTTCTATTTGTTACTGCACAGAGTTTTTTTTTAAAAATTGAGTTTGTTATG
TGGATTCAATACTCAGATAGAGCTCTTTAATTTTTTTACAGTGACCTCATGAATCATAAC
TTGCCTTACAGACAATGGATGGAATCGTACAGAACATGTTTACATTCAATTGTAATTGTGG
AAATAATAATAGGATGGATTGGAATGGATT CATAGCTCTGGTGAAGTGCATACACTGGT

ACAAGAGAAGAAAGATCTCTGCACTGAATCAAATACTCACAGCCTTGGCTTTCTCCAGAA
TCTACCTTCTTTTAACAGTATTTACTGTTATAGCAGTGTCTACGCTATACACACACGTGT
TGGTAACTAGAAGAGTGGTAAACTGATTAATTTCCATTTGCTTTTCAGCAATCATTTTA
GCATGTGGCTTGCTGCATGCCTTGGCCTTTATTATTTTCTTAAAATAGCTCATTTTCCTA
5 ACTCTATTTTTGTTTACTTAAAGATGAGAATTAACCAGGTGGTTTCAGGGACTTTGCTCA
TGTCTTTGGGCCTCTTGTTTCTAAACACTCTGCTGATAAACTCATAATTGATACCAAGA
TAGATGACTACAGAGAACATCTACTGTATGATTTCACTTCGAATAATACTGCTTCATTTT
ACAGGGTTATTTTAGTCATTAACAACGTATTTTACATCTATACCCTTTACACTTTCCC
AGTCCACTTTTCTCCTGCTCATCTTCTCCCTGTGGAGACATTACAAGAAGATGCAACAGC
10 ATGCACAAAGATGCAGAGATGTCCTTGACAGATGCCACATCAGAGTCTTGCAAACCATGG
TCACCTATGTCCTACTCTGTGCCATTTTCTTTCTGTCTCTTTCCATGCAAATTTTGAGGA
GTGAGTTGTTGAAGAACATTCTTTACGTTAGGTTCTGCGAGATTGTTGCAGCAGTTTTTC
CTTCAGGACACTCCTGTGTCTTAATCTGTAGAGACACAAACCTGAGAGGGACCTTTCTTT
CTGTGCTATCGTGGCTGAAGCAGAGGTTTACATCATGGATTCCTAACATAAATTGCAGAT
15 CATCTTGCATATTCTAAAAGAACTGAG

SEQ ID NO:162

Mouse T2R30 amino acid sequence

20 MTYETDTTLMMLVAVGEALVGILGNFIALVNFMGWMKNRKIASIDLILSSVAMSRICLQC
IILLDCIILVQYPDTYNRGKEMRTVDFFWTLTNHLSVWFATCLSI FYLFKIANFFHPLFL
WIKWRIDKLILRTLACVLIISLCFSLPVTENLSDDFRRCVKTKERINSTLRCKVNKAGHA
SVKVN LNLVMLFPFSVSLVSFLLLILSLWRHTRQIQLSVTGYKDPSTTAHV KAMKAVISF
25 LALFVVYCLAFLIATSSYFMPES ELAVIWGELIALIYPSSHFILILGSSKLKQASVRVL
CRVKTMLKGKKY

SEQ ID NO:163

30 Mouse T2R30 nucleotide sequence

AAAAATGTTTCATTGTTTATCTAAAATTCAAATTTAACTGAGTGCCCTACATTTTTATTTA
TTCAATCTAGTAGCTGTACTGAGGTTATTAGTGTGATTTCTGAAGCCCAAATTTGTAAAA
CTTAGCCTCAGATAAACAGCTTGAGACCATGGAAAGTAATTTGGTAAATTTGCATCTTAG

CAAAAAGAACACCTACAAATTTGCTCTAGACATCTAGACTGTATCAAACAGTGAATATGA
 AAATATCATAACAGGATATAGCCTTTAGTATTGAAGACAGGTTTCATCTATATTAAACCTG
 CATAACATACCTAAAAGACTAAGTCAATATCCCACAAACATATTTGCACTATCATGTCTAT
 TGAAACACTATTCATAGTAGCTAAAATATGGCACAAAACCTAGACATTCATCAATAGATGA
 5 ATCAATAAAGCAAATGTACATACACAAGATGAAATTGTATTCAGGCATAAAGAAGAATGC
 AGTCATGTTCATTAGCAAAAACATAAACAGAATTGGAGGTCATTGTGATAATTGAAATAAA
 CCAGACCTGGAAAAACAAAACCTGTGTAATTTTTCTGAAGTAGAGAATATACTCTTGGA
 TGGATAGATGGGTACTGTTATAGTATAAAATGTGTGTGTGTGTGTGTGTGTGTGTGTGTG
 TATTTTCATGAAAGCAAGAATGGGACTGCTTAGAGAAAGAAAAGGACAAACAGGTGAAGGG
 10 GTGAAAGAAAAAGGCAATGACAAGGAGTAATGATATGAGCAAAGTACCATTATTAAACAT
 GTGACAATATTATATAGAAACACATGATTTTGTGTGCCTACCAAACCTGGATAATAATTT
 TTAAATGTATCTATTAAAAGGAAAGAAAAGAAAGTGCAAGCCCAGGAAAGGGAGAAAAG
 GAAACAATGAGAGAGAAATGGAAATGGTGAGAAGTGAAGAGAACAAAAAGAAATGGAGT
 AAGTGTGGCCAGGAATGAAGGATCTCAGCTATAGTTATCCCAGTACGGTAATACAAATCT
 15 GTGACTCCAGCACTTGACAAGGCTGAGAGATGTGAGAGAGGGCCAGTTAACAACCACTCT
 GGGCTTATTCCAAGAGATAAGAAGATTGGGGGAAAGTATGTAGAAGGGTTTGAGGGGAAG
 AGAGAGAAGAGGGAAATGATGTAATGATAGTACAAATCAAAGTTATTTTTCTAAAAAA
 GCAATGGGACAGGAAACCAACCTAACAAGTAAAGGTGCTTGGTTCACAAGACCAGCAACC
 TGAGTGCATCCTTGCTAGAATGAAATTGGCCTTACTCTGGAAAGCTTACTTCCTCAGTGT
 20 ATTCATTGTTAAAATTCATGTGGAGATTTTAAAGAAAAAAGGAAAAAAAAGTTAAATGG
 TAGATTTGTGTAGGGGAATATTCCCCTAATTAATTGATTAGATAATAAAGATGACAAGCA
 AATTGCTGTGCAAAAAGGAAGACAAGGTCTAAGAGGGGAAGAGGGGACACGGGAGGAAAA
 AAAACGGCCCTTTTTTAAAGCAAGGTGGGGAGTGAGGGAAGCGAGATGTAGACAGGGAACT
 GTTAGACCTGGTGGCAGCTTCTGCCACCTGAAGATTTTCAACATAGTATAGTTCATGAGT
 25 TTAGGAAGATATGTTCCCTGCCCAGCGGTTGTATCATCTGTTGATTTTAAACTAAGATTG
 TCTGGTGTTTTCCATTTGCGGAGACTCAAGTAGACCAAAGGGAAAGAATGAATTC

SEQ ID NO:164

30 Mouse T2R31 amino acid sequence

MYMILVRVAFITGMLGNMFIGLANCSDWVKNQKITFINFIMVCLAASRISSVLMLFIDAT
 IQELAPHFYYSYRLVKCSDIFWVITDQLSTWLATCLSI FYLFKVAHISHPLFLWLKWRLR
 GVLVFLVFSLFLLLISYFLLLETLPWGDYVTLKNNLTLFSGTIKTTAFQKIIVFDIIY

LVPFLVSLASLLLLFLSLVKHSRSLDLISTTSEDSRTKIHKKAMKMLVSFLILFIIHIF
MQLARWLLFLFPMSRPINFILTLNIFALTHSFILILGNSNLRQRAMRILQHLKSQLOELI
LSLHRFSSLY

5

SEQ ID NO:165

Mouse T2R31 nucleotide sequence

CTGCAGCTTTCTAGAAATCTCACCAGAATGTCTTTGTGCAGCTTTAATAGTTCCTGGTTA
10 TACCTTGTACATTATAAGCTAAGACATCTTTGGTGCCACAATATACTCTCACTAATCAG
AGAGATTAGACAGAAAAATAAGTTTCTTAACAACGTGTTTAGATAGGGTCATGAAATGAC
ATAAAACACCAATGCTAAGGCAATCCATTATGTTTTCTCATGAGGAGCCCATATGTACAC
TTGAGTGTGTCTTATTATTTCCCTGAGTGATTTTGTAATTTTATTAAACACTTAACTGTG
ATTCATACTAGTTAGTTCTGAAATTCTTTTCTTCATCAAAGCCATTAATCCTGGGGTTTT
15 TTAAATGGAGAACCCCAAACAAAGTGAAATGTTGTGTGTGGAGCAGGCTGTCTTCCCAC
ACACTACCATGAGATGCTCATTCTGTAATTGTTCCCGGAATAGGAAATGCCCTGAATTC
AGGCACACAAGAGCTAGTCTGTGCACCATGTCTGGTTCCTGCATTAATACCCACTTTTGT
CACGAAGCTTCATTGATTCGCATCTTCAGAAGCTGGTATCATTATTAGTTTCTTTCTCTCA
GGTGACTCTGGnCCAAAATATTAnGGCGCCCTTTAAAAAAGTAAAACTACAAAATTTCTT
20 TATAATTTTCTTTAAGTTTGTTATAATATAGCATGACCTACACACACACACACACACA
CACACACACACACACACAAGTATGCCTCTCCTTTCCTTCTAAAAATCTCACTTAAAGC
AATTGTTTAGCTGTCTTCGAAGTCTAGACTGCCACTGTCGTGCTTCTAGCCAAAACAAAT
GCAACACATAAAATGATAGAGCTCAAACTTAGGAATCTATTTAACTGTGAAGATCACGC
AAGCAAACCTGAGAAACCTCTAGAAGGAAACCACAGCAAATCACTGGAGAGAAGGTGTTA
25 ATCTAGTAAGAATAGTTTTTATTTTGGGTATCCTTTTGTAGATTGGTTAGTTCATCCAAA
ATCCAACCTTGTTAGTTCTTCATAAATTGTAAGTGTCTCCAACATCAAAGCACCCTTCTC
TCTTTTCCCCTGTATGAAGATGCTTTAAGTACAGAGTTACTCTTTTCTGTACTGACAGT
AATTTAAAAAAATTGTTCACTCATTCTTTTTTGGTGTTGTTATTCTGTGTTCCCTCAATGT
TATCTTTTTTTTTTCAAACTTTCTTTTATAAAAAGTCATACACATAGCAAATGCAGTGC
30 ATGTTTATGGAATCCATAACTAATTATGAGACTTCTCCTAGTACTTTCTTTGAACAGT
AACAAAGATATCTGCTTCTACAGAGTGCAGTGTTTCAGGTGAGGAGGAACATATTATACA
AATCAGTGAAAAAAAATCTGATTCAAATTTGTATTTTAATATATTTGACTTTATCACTT
CAGATATTACATCAATGGGAATTTTGAAGGCACACAAGTGATGATGTGGGCATAGAGACT
GTCTGTACTAGAATTTAATATTTCTTTTAAATATCTTTAAATAAAAATATGATGCTGTAT

TCATAAACAGATCTTTATAGATTAAGTATGAGATTAAAGTTGGAAAAACAAAAGACAAAA
ACCTAGGACTAAGAATTTCTTAAGTATGTGTGAATATCAACCTAATGGAGGAAGTTTCC
AATCAAAGCTGAAATTACAGTAAAAAGGAGGAAGATAAATATGGAAAAGGATGATTTTCT
GTGGAAGTTTGTGTTGAGAACTGATCCACGAGACAAATTGCTAG**AAG**TGTGGATTCCCTTT
5 TACTATTCAACTGCTTATAGGACTGGATCAA**ATGTATATGATACTGGTAAGAGCAGTATT**
TATAACTGGAATGCTGGGAAATATGTTCAATTGGACTGGCAACTGCTCTGACTGGGTCAA
GAACCAGAAAATCACCTTCATCAACTTCATCATGGTCTGTTTGGCAGCTTCCAGAATCAG
CTCTGTGCTGATGTTATTTATTGATGCAACCATAACAAGAACTAGCGCCTCATTTCTATTA
TTCTTACCGTCTAGTAAAATGCTCTGATATATTCTGGGTATAACTGATCAACTATCAAC
10 **ATGGCTTGCCACCTGCCTGAGCATATTCTACTTATTCAAAGTAGCCACATTTCCCATCC**
CCTTTTCCTCTGGTTGAAGTGGAGATTGAGAGGTGTGCTTGTTGTTTTCTTGATTTTTC
TTTGTTCTTATTGATTTCTTATTTTCTACTGCTTGAAACACTTCCTATTTGGGGAGATAT
TTATGTAACCTTAAAAACAATCTGACCTTATTTTCAGGTACAATTAAGACCACTGCTTT
TCAAAGATAATTGTTTTTGATATAATATATTTAGTCCCATTTCTTGTTGCCCTAGCATC
15 **ATTGCTCCTTTTATTTTTGTCCTTGGTGAAACACTCCCGAAGCCTTGACCTGATTTCTAC**
CACTTCTGAAGATTCAGAACCAAGATTCATAAGAAGGCCATGAAAATGCTGGTGTCTTT
CCTCATTCTCTTTATAATTCACATTTTTTTTCATGCAGTTAGCACGGTGGTTATTATTTTT
GTTTCCAATGAGCAGGCCAATTAATTTTCATCTTAACATTAAATATCTTTGCCTTAACTCA
CTCATTTATTCTCATCCTGGGAAATAGCAATCTTCGACAGAGAGCAATGAGGATCCTGCA
20 **ACATCTTAAAGCCAGCTTCAAGAGCTGATCCTCTCCCTTCATAGATTCTCCAGTCTTTA**
CTAGAGGAACAGCTTAACAGGGAGACTTGGAAGGTCACTGGCAAATTATTCTTCTTTGAT
TTCTTTTAAGTACTGCTGAACATATATGAACTGTCCCCAGAGCATAGTGCTATCTTATGA
GAAGGATATCATCTCACAGTCTGGTTATAAAACACAAACCAATCTTTTTATAATTTCTTT
ACAGCATTGCTAATAAAAGACTTGTAGTCTCAAATATTTTAAAGAGAATAATTAATTTTA
25 **TAGGCAAAAGGTATGAAATTACAATTCACAGGGAAGGTTTCATGACTCCTTAGATATTTAA**
GTTAATTGTAAGCCACAATAGGCAGAAGATGAGCAAAATGTTGATAGGAGATAAATAAAA
TCTAAAGTTACGGAGAAAAAAAACATCAACTTGCCTTTTAGATTACTTTAAAGCTCTCTC
TCTCGCTCTCTCTCTGTATCTACTTACTTTATATATACAAATGTTTTGTCTGCATGTA
TTTCTTTGCACCATATAAATGTCTAAGTATCCAGAAnGTCAGCAGAGGGCATCAAATTCT
30 CTGGAAAGAGAGTTACAAATTGCTGTGGGTAACTGGGTGCTGGGAACTAACCTGAGTC
CTCTGCCACAGCAACTGCTCTTCCCTGCTGAGTCATGTTTTAAGTCTCCACAACCTTAAAC
TCATTGTTGATGTGGTCATTGCATAATGATGAATTTACATTCTAAGGTTTGTATCATAGG
TAGGAGGGCTGGTTTTAATCATATTCTAATGTTCTTATACAAACCCAGGTTTTGTAAGAG
ACTGTATTCTATCATGAGACTCTTTCCCCACACCGCCAATGTAACATTTTTATTAATTTT

GAGGGGAATTTTATACAGTGTACCCTGATCACCCCTTGCTTCCCCTCCTTGCAGGTCTAC
 CCTCCCACCATTGCTCAATCCCCCTAAAAGAGAGAGAAACAAACCATGTCCAATTTGTG
 TTGGACACATACTCAGTGGAACATGGCCAAACCCCTAGTGAGCAGTTCCTTAAAGAAAAC
 TAAGCTGCCTCCCCACCACTACCACCATAGGGCATTAACTGTGAAGAGCTACACTTTAGC
 5 TATTTTATCACCAATTTAAAAGACTGTCTTCAATAGCTTCCTCTATGGACTGTTTCTGGT
 TTTAGTGGGACAGGGAGAAGGGGTCAAGAGGTTGTCACAGAACTTTTGATGTCTCTTAT
 TCTCAGTTAAAGTCCACTGCAAAGAAGTCTGCTGGCTCTAATAAAGCTTGCAACAGCAT
 GGGCCAGTGACATCATCATGATTTCTGGCAACAATATGGACCACAAATATCATGGCTCAG
 GTGGCATTACGGACCACAGACATCAACATGGTCTCTGGCAGCAAGAACCAGAATCTTTTG
 10 AGGAGGCTTCATTCAGAAAATGAATTTTTCTTCATCCCAGATATACTGATGTTGCTCAAT
 CAGAGTATTAGTATGGTTGGGCACCATATTTGGGGACAGGACCTTCAATATTTCCAGGCT
 GCTGTGTAACACATTATCTTTAGTGTGAGGTGCCCTTAGTGTGAGGACATGACCATCATG
 TATGCGCCTGTGGGCAGAAATACATCTTTGTACTTTCTTACACCTAGCAGGGTGAGTAGC
 AGGAGCAGCGGCATTAATACTTCCATACCTCTGGGCAGCCTATCAGGTATCATCTAGGCA
 15 AGGTAAGCCCAGTAGTGGCCCAAGGCTCCTGGTGTCTACTTGGCAACAACATGCTCCTTT
 GTCTGCACTGCCATATCTATGGCTGGTTCTCCATCCCTAGTTCTGCTTCTCTCAGGTTTT
 ATACGACTCTATTCCACATTCTATTTTTCCAGTTCCATGAAACCAGTGTTTAAAAGTATC
 ATCCCATAAGACCGGCCTTTTAAAGGTTATTCTGGAGATATTGCAGAGTCTGCAG

20

SEQ ID NO:166

T2R Family Consensus Sequence 1

E (F/A) (I/V/L) (V/L) G (I/V) (L/V) GN (G/T) FI (V/A) LVNC (I/M) DW

25

SEQ ID NO:167

T2R Family Consensus Sequence 2

30 (D/G) (F/L) (I/L) L (T/I) (G/A/S) LAISRI (C/G/F) L

SEQ ID NO:168

T2R Family Consensus Sequence 3

NH (L/F) (S/T/N) (L/I/V) W (F/L) (A/T) T (C/S/N) L (S/N/G) (I/V)

5 **SEQ ID NO:169**

T2R Family Consensus Sequence 4

FY (F/C) LKIA (N/S) FS (H/N) (P/S) (L/I/V) FL (W/Y) LK

10

SEQ ID NO:170

T2R Family Consensus Sequence 5

LLI (I/F/V) SLW (K/R) H (S/T) (K/R) (Q/K) (M/I) (Q/K)

15

SEQ ID NO:171

T2R Family Consensus Sequence 6

20 HS (F/L) (I/V) LI (L/M) (G/S/T) N (P/S/N) KL (K/R) (Q/R)

WHAT IS CLAIMED IS:

1. A method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of:
- (i) contacting a taste transduction G-protein coupled receptor polypeptide with the compound, the polypeptide comprising greater than 50% amino acid identity to a sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168; SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171; and
- (ii) determining the functional effect of the compound upon the polypeptide.
2. The method of claim 1, wherein the polypeptide has G-protein coupled receptor activity.
3. The method of claim 1, wherein the functional effect is a chemical effect.
4. The method of claim 1, wherein the functional effect is a physical effect.
5. The method of claim 1, wherein the functional effect is determined by measuring binding of the compound to an extracellular domain or a transmembrane region of the polypeptide.
6. The method of claim 1, wherein the functional effect is determined by measuring binding of radiolabeled GTP to the polypeptide.
7. The method of claim 1, wherein the polypeptide is recombinant.
8. The method of claim 1, wherein the polypeptide is from a rat, a mouse, or a human.
9. The method of claim 1, wherein the polypeptide is expressed in a cell or cell membrane.
10. The method of claim 9, wherein the functional effect is measured by determining changes in the electrical activity of a cell expressing the polypeptide.

11. The method of claim 9, wherein the functional effect is determined by measuring changes in intracellular cAMP, cGMP, IP3, or Ca²⁺.

12. The method of claim 11, wherein a change in intracellular Ca²⁺ is detected by detecting a change in FURA-2 dependent fluorescence in the cell.

5 13. The method of claim 9, wherein the cell is a eukaryotic cell.

14. The method of claim 13, wherein the cell is an HEK-293 cell.

15. The method of claim 9, wherein the polypeptide is a fusion protein comprising at least about 20 consecutive N-terminal amino acids of a rhodopsin protein.

10 16. The method of claim 15, wherein the rhodopsin protein is a bovine rhodopsin.

17. The method of claim 9, wherein the cell comprises Gα15.

15 18. The method of claim 9, wherein the polypeptide is contacted with the compound in the presence of a bitter tastant, and wherein a difference in the functional effect of the bitter tastant on the cell in the presence of the compound and the functional effect of the bitter tastant on the cell in the absence of the compound indicates that the compound is capable of modulating taste signaling in taste cells.

19. The method of claim 1, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID

20

25

NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

10 ~~20.~~ A method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of:

(i) contacting a taste transduction G-protein coupled receptor polypeptide with the compound, the polypeptide comprising greater than 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164; and

(ii) determining the functional effect of the compound upon the polypeptide.

21. The method of claim 20, wherein the polypeptide has G-protein coupled receptor activity.

5 22. The method of claim 20, wherein the functional effect is a chemical effect.

23. The method of claim 20, wherein the functional effect is a physical effect.

10 24. The method of claim 20, wherein the functional effect is determined by measuring binding of the compound to an extracellular domain or a transmembrane region of the polypeptide.

25. The method of claim 20, wherein the functional effect is determined by measuring binding of radiolabeled GTP to the polypeptide.

26. The method of claim 20, wherein the polypeptide is recombinant.

15 27. The method of claim 20, wherein the polypeptide is from a rat, a mouse, or a human.

28. The method of claim 20, wherein the polypeptide is expressed in a cell or cell membrane.

20 29. The method of claim 28, wherein the functional effect is measured by determining changes in the electrical activity of a cell expressing the polypeptide.

30. The method of claim 28, wherein the functional effect is determined by measuring changes in intracellular cAMP, cGMP, IP3, or Ca^{2+} .

31. The method of claim 30, wherein a change in intracellular Ca^{2+} is detected by detecting a change in FURA-2 dependent fluorescence in the cell.

25 32. The method of claim 28, wherein the cell is a eukaryotic cell.

33. The method of claim 32, wherein the cell is an HEK-293 cell.

34. The method of claim 28, wherein the polypeptide is a fusion protein comprising at least about 20 consecutive N-terminal amino acids of a rhodopsin protein.

35. The method of claim 34, wherein the rhodopsin protein is a bovine
5 rhodopsin.

36. The method of claim 28, wherein the cell comprises Gα15.

37. The method of claim 28, wherein the polypeptide is contacted with the compound in the presence of a bitter tastant, and wherein a difference in the functional effect of the bitter tastant on the cell in the presence of the compound and the
10 functional effect of the bitter tastant on the cell in the absence of the compound indicates that the compound is capable of modulating taste signaling in taste cells.

38. The method of claim 20, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID
15 NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID
20 NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID
25 NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID
30 NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID

NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

39 A method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of:

- 5 (i) contacting a polypeptide comprising an extracellular domain or a transmembrane region of a taste transduction G-protein coupled receptor with the compound, the extracellular domain or transmembrane region comprising greater than 60% amino acid sequence identity to the extracellular domain or transmembrane region of a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:1, 10 SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164; and 25
- (ii) determining the functional effect of the compound upon the 30 extracellular domain or transmembrane region.

40. The method of claim 39, wherein the polypeptide comprises an extracellular domain or a transmembrane region that is covalently linked to a heterologous polypeptide, forming a chimeric polypeptide.

41. The method of claim 39, wherein the polypeptide has G-protein coupled receptor activity.

42. The method of claim 39, wherein the polypeptide is linked to a solid phase.

43. The method of claim 42, wherein the polypeptide is covalently linked to a solid phase.

44. The method of claim 39, wherein the functional effect is determined by measuring binding of the compound to the extracellular domain or transmembrane region.

45. The method of claim 39, wherein the polypeptide is recombinant.

~~46.~~ An isolated nucleic acid encoding a taste transduction G-protein coupled receptor, the receptor comprising greater than 50% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

47. The nucleic acid of claim 46, wherein the receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

48. The nucleic acid of claim 46, wherein the nucleic acid encodes a receptor that specifically binds to polyclonal antibodies generated against a polypeptide having a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81; SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID

NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, but not to polyclonal antibodies generated against a

5 polypeptide having a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID

10 NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID

15 NO:74, SEQ ID NO:75, and SEQ ID NO:76.

49. The nucleic acid of claim 46, wherein the nucleic acid encodes a receptor that has G-protein coupled receptor activity.

50. The nucleic acid of claim 46, wherein the nucleic acid encodes a receptor comprising an amino acid sequence selected from the group consisting of SEQ

20 ID NO:77, SEQ ID NO:79, SEQ ID NO:81; SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID

25 NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

51. The nucleic acid of claim 46, wherein the nucleic acid comprises a

30 nucleotide sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID

NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165.

52. The nucleic acid of claim 46, wherein the nucleic acid is from a rat or a mouse.

53. The nucleic acid of claim 46, wherein the nucleic acid encodes a chimeric polypeptide comprising an extracellular domain or a transmembrane region linked to a heterologous polypeptide.

54. An expression vector comprising the nucleic acid of claim 46.

55. An isolated cell comprising the vector of claim 54.

56. An isolated nucleic acid encoding a taste transduction G-protein coupled receptor, wherein the nucleic acid is amplified by primers that selectively hybridize under stringent hybridization conditions to the same sequence as degenerate primer sets encoding amino acid sequences selected from the group consisting of:

20	(1)	E(F/A)(I/V/L)(V/L)G(I/V)(L/V)GN(G/T)FI(V/A)LVNC(I/M)DW (SEQ ID NO:166);
	(2)	(D/G)(F/L)(I/L)L(T/I)(G/A/S)LAISRI(C/G/F)L (SEQ ID NO:167);
	(3)	NH(L/F)(S/T/N)(L/I/V)W(F/L)(A/T)T(C/S/N)L(S/N/G)(I/V) (SEQ ID NO:168);
	(4)	FY(F/C)LKIA(N/S)FS(H/N)(P/S)(L/I/V)FL(W/Y)LK (SEQ ID NO:169);
25	(5)	LLI(I/F/V)SLW(K/R)H(S/T)(K/R)(Q/K)(M/I)(Q/K) (SEQ ID NO:170); and
	(6)	HS(F/L)(I/V)LI(L/M)(G/S/T)N(P/S/N)KL(K/R)(Q/R) (SEQ ID NO:171).

57. The nucleic acid of claim 56, wherein the receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

58. The nucleic acid of claim 56, wherein the nucleic acid encodes a receptor that specifically binds to polyclonal antibodies generated against a polypeptide having a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81; SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ

ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID
 NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID
 NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID
 NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID
 5 NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID
 NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID
 NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID
 NO:162, and SEQ ID NO:164, but not to polyclonal antibodies generated against a
 polypeptide having a sequence selected from the group consisting of SEQ ID NO:1, SEQ
 10 ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13,
 SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ
 ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID
 NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID
 NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID
 15 NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID
 NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID
 NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID
 NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID
 NO:74, SEQ ID NO:75, and SEQ ID NO:76.

20 59. The nucleic acid of claim 56, wherein the nucleic acid encodes a
 receptor that has G-protein coupled receptor activity.

 60. The nucleic acid of claim 56, wherein the nucleic acid encodes a
 receptor comprising an amino acid sequence selected from the group consisting of SEQ
 ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID
 25 NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID
 NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID
 NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID
 NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID
 NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID
 30 NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID
 NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID
 NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

61. The nucleic acid of claim 56, wherein the nucleic acid comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165.

62. The nucleic acid of claim 56, wherein the nucleic acid is from a rat or a mouse.

63. The nucleic acid of claim 56, wherein the nucleic acid encodes a chimeric polypeptide comprising an extracellular domain or a transmembrane region linked to a heterologous polypeptide.

64. An expression vector comprising the nucleic acid of claim 56.

65. An isolated cell comprising the vector of claim 64.

~~66.~~ An isolated nucleic acid encoding a taste transduction G-protein coupled receptor, the receptor comprising greater than 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81; SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

67. The nucleic acid of claim 66, wherein the nucleic acid encodes a receptor that specifically binds to polyclonal antibodies generated against a polypeptide having a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81; SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, but not to polyclonal antibodies generated against a polypeptide having a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76.

68. The nucleic acid of claim 66, wherein the nucleic acid encodes a receptor that has G-protein coupled receptor activity.

69. The nucleic acid of claim 66, wherein the nucleic acid encodes a receptor comprising an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81; SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID

NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

5 70. The nucleic acid sequence of claim 66, wherein the nucleic acid comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID NO:106, SEQ ID NO:108, SEQ ID
10 NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID
15 NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165.

71. The nucleic acid of claim 66, wherein the nucleic acid is from a rat or a mouse.

72. The nucleic acid of claim 66, wherein the nucleic acid encodes a chimeric polypeptide comprising an extracellular domain or transmembrane region linked
20 to a heterologous polypeptide.

73. An expression vector comprising the nucleic acid of claim 66.

74. An isolated cell comprising the vector of claim 73.

~~75.~~ An isolated nucleic acid encoding a taste transduction G-protein coupled receptor, wherein the nucleic acid specifically hybridizes under highly stringent
25 conditions to a nucleic acid having a sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID
30 NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID

NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165, but not to a nucleic acid having a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, and SEQ ID NO:63.

~~76.~~ An isolated nucleic acid encoding a taste transduction G-protein coupled receptor, the receptor comprising greater than 60% amino acid sequence identity to a polypeptide having a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, wherein the nucleic acid selectively hybridizes under moderately stringent hybridization conditions to a nucleic acid having a nucleotide sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID

NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165, but not to a nucleic acid having a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, and SEQ ID NO:63.

77. An isolated taste transduction G-protein coupled receptor, the receptor comprising greater than 50% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

78. The isolated receptor of claim 77, wherein the receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

79. The isolated receptor of claim 77, wherein the receptor has G-protein coupled receptor activity.

80. The isolated receptor of claim 77, wherein the polypeptide is covalently linked to a heterologous polypeptide, forming a chimeric polypeptide.

81. The isolated receptor of claim 80, wherein the chimeric polypeptide has G-protein coupled receptor activity.

82. An antibody that selectively binds to the receptor of claim 77.

83. An isolated taste transduction G-protein coupled receptor, the receptor comprising greater than 60% amino acid sequence identity to a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81; SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID

NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

5 84. The isolated receptor of claim 83, wherein the receptor specifically binds to polyclonal antibodies generated against a polypeptide having a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81; SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID
10 NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID
15 NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, but not to polyclonal antibodies generated against a polypeptide having a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ
20 ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID
25 NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76.

85. The isolated receptor of claim 83, wherein the receptor has G-protein coupled receptor activity.

30 86. The isolated receptor of claim 83, wherein the receptor has an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81; SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID

NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

87. The isolated receptor of claim 83, wherein the receptor is from a rat or a mouse.

88. The isolated receptor of claim 83, wherein the polypeptide is covalently linked to a heterologous polypeptide, forming a chimeric polypeptide.

89. The isolated receptor of claim 88, wherein the chimeric polypeptide has G-protein coupled receptor activity.

90. An antibody that selectively binds to the receptor of claim 83.

91. An expression cassette comprising a polynucleotide sequence that encodes a human taste transduction G protein coupled receptor, operably linked to a heterologous promoter, wherein the receptor comprises an amino acid sequence comprising greater than 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76.

92. The expression cassette of claim 91, wherein the polynucleotide encodes a receptor comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76.

93. An isolated eukaryotic cell comprising the expression cassette of claim 91.

[-Gα₁₅ + agonist] [+Gα₁₅ + agonist] [+Gα₁₅ - agonist]

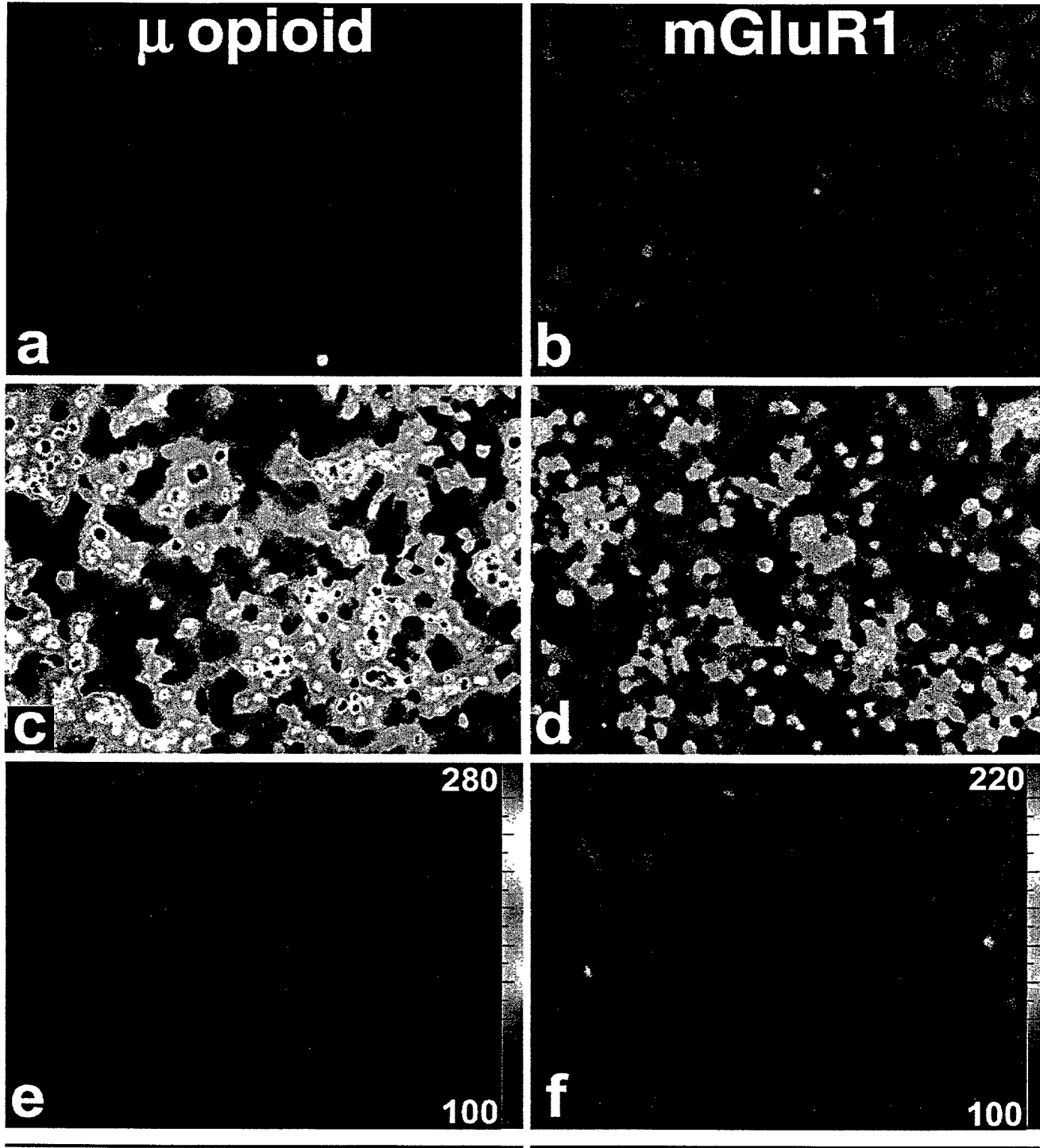


Figure 1

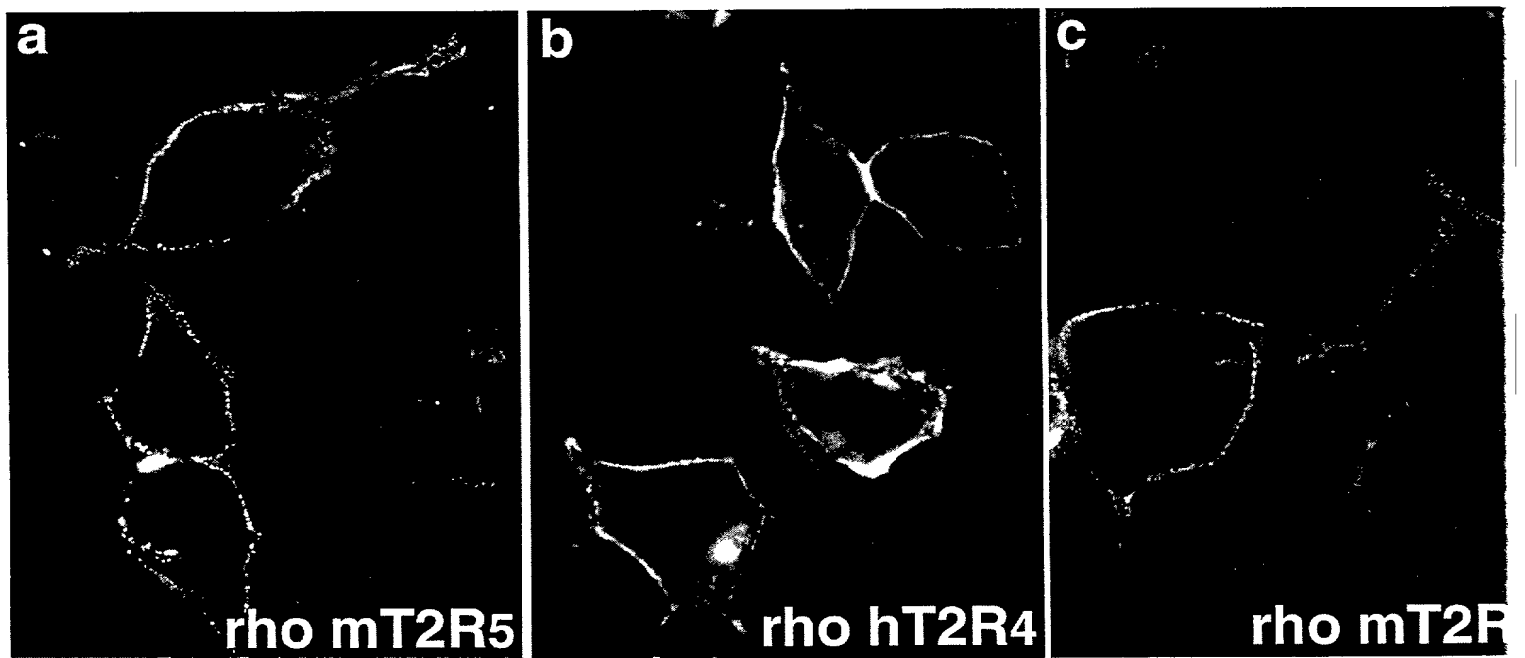


Figure 2

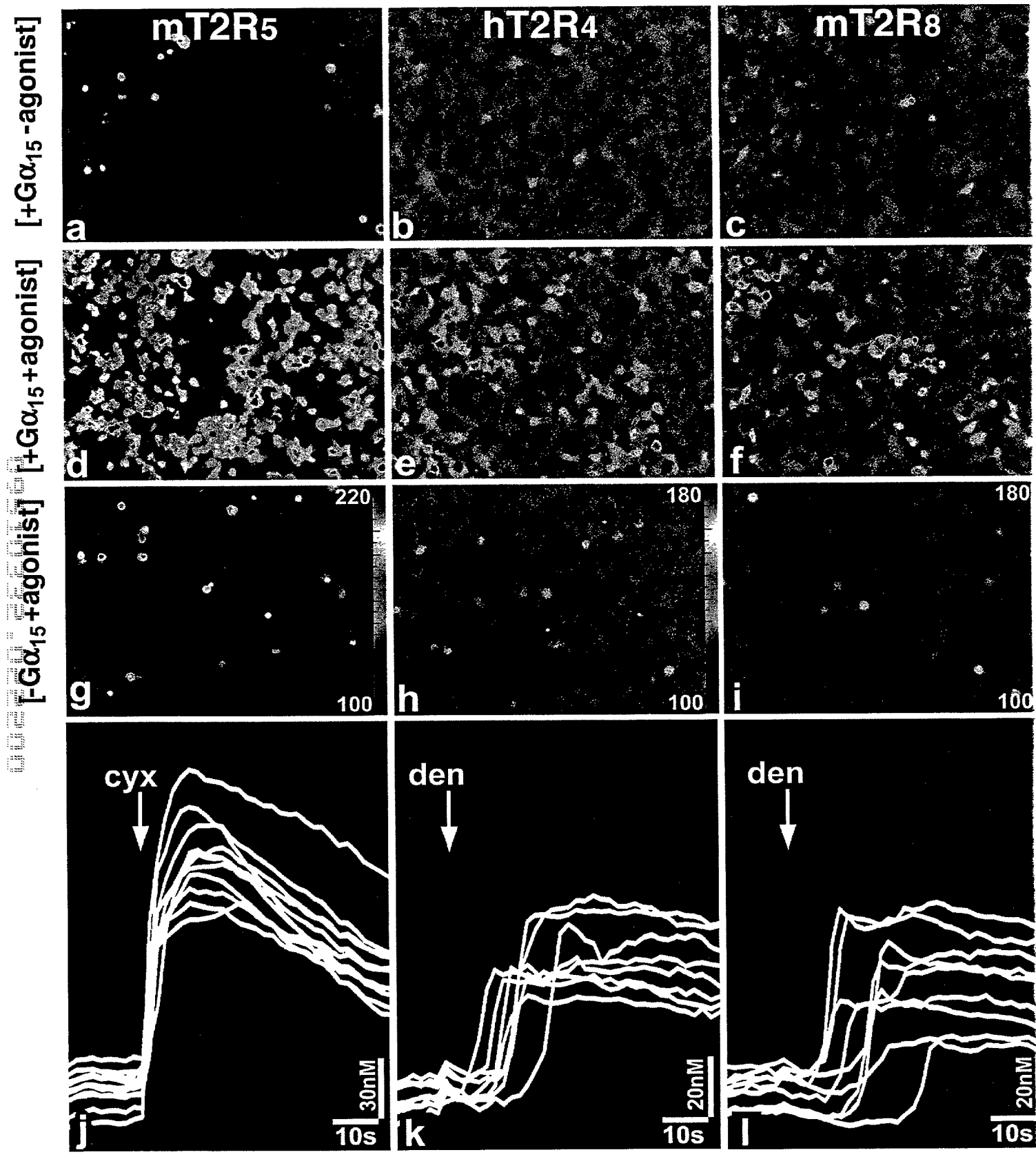


Figure 3

Figure 4

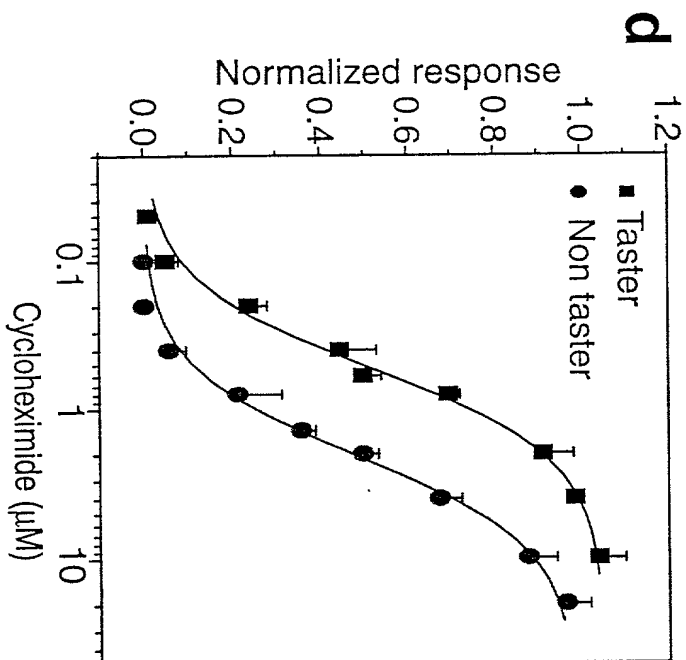
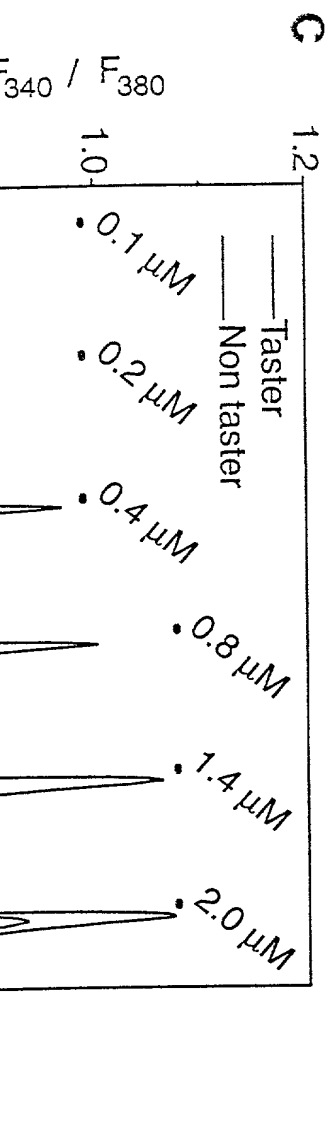
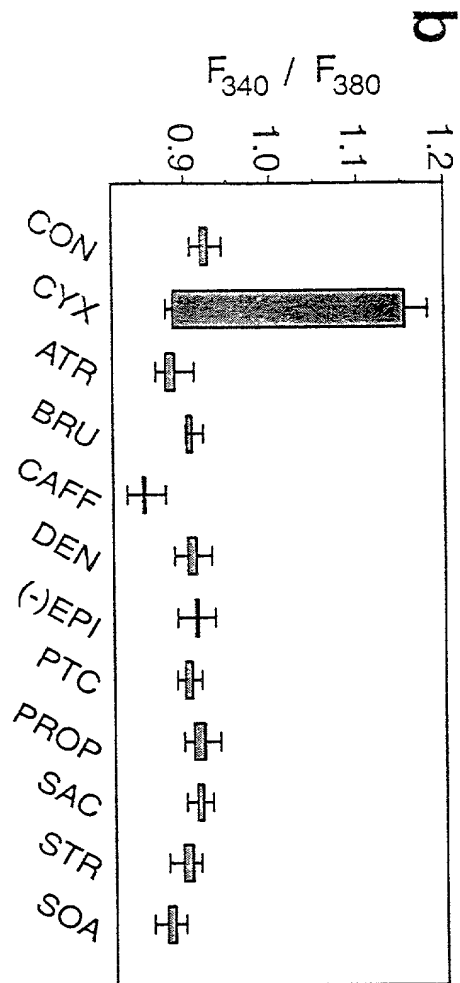
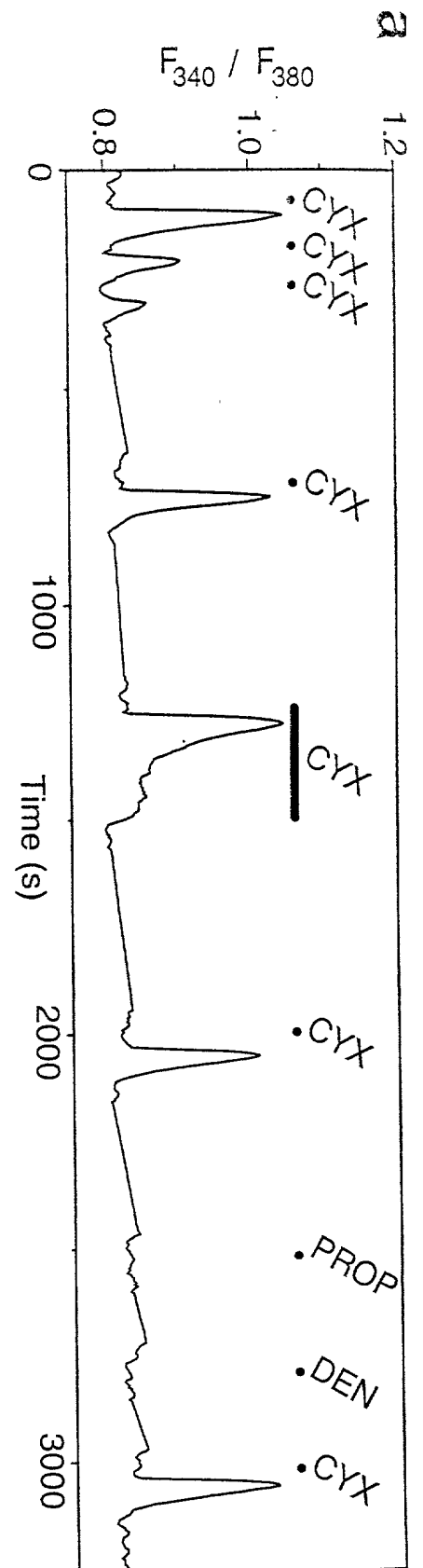
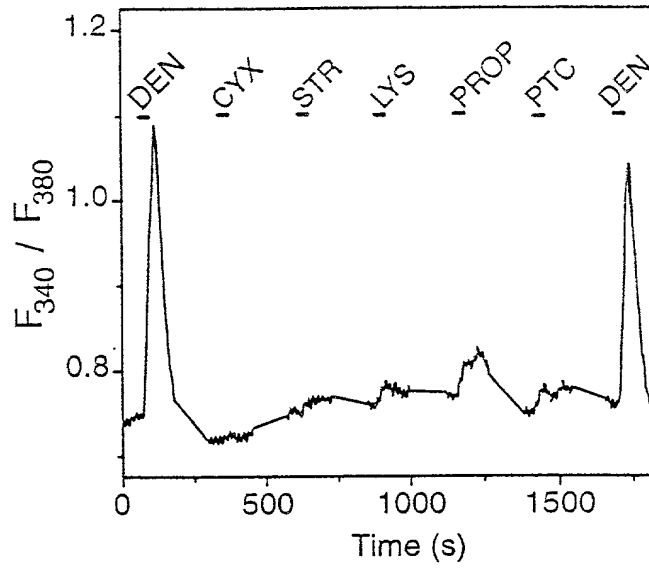
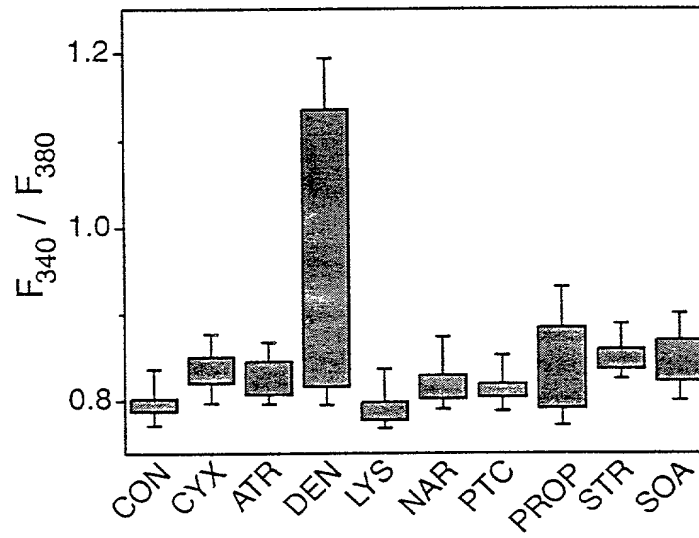


Figure 5

a



b



c

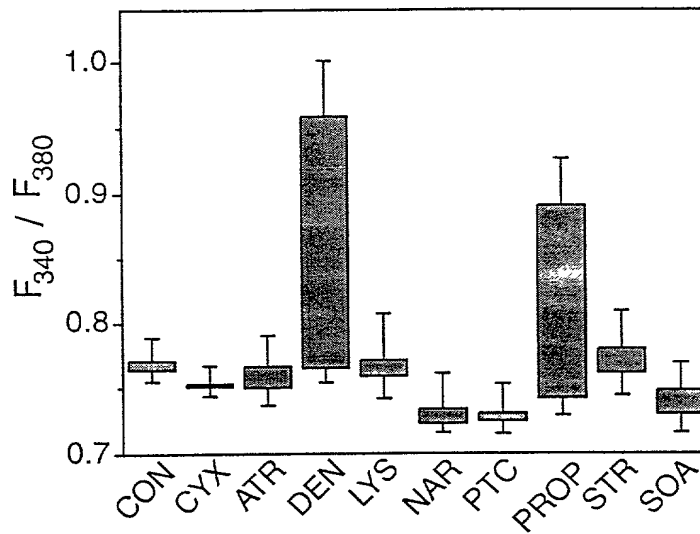


Figure 6

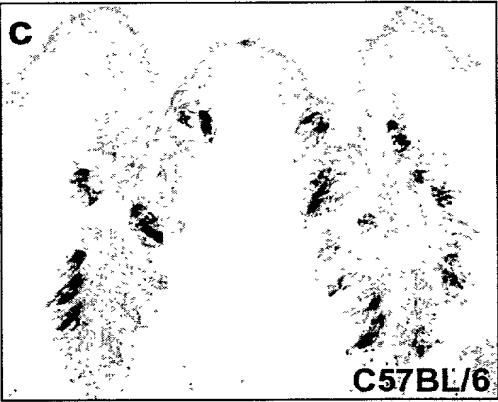
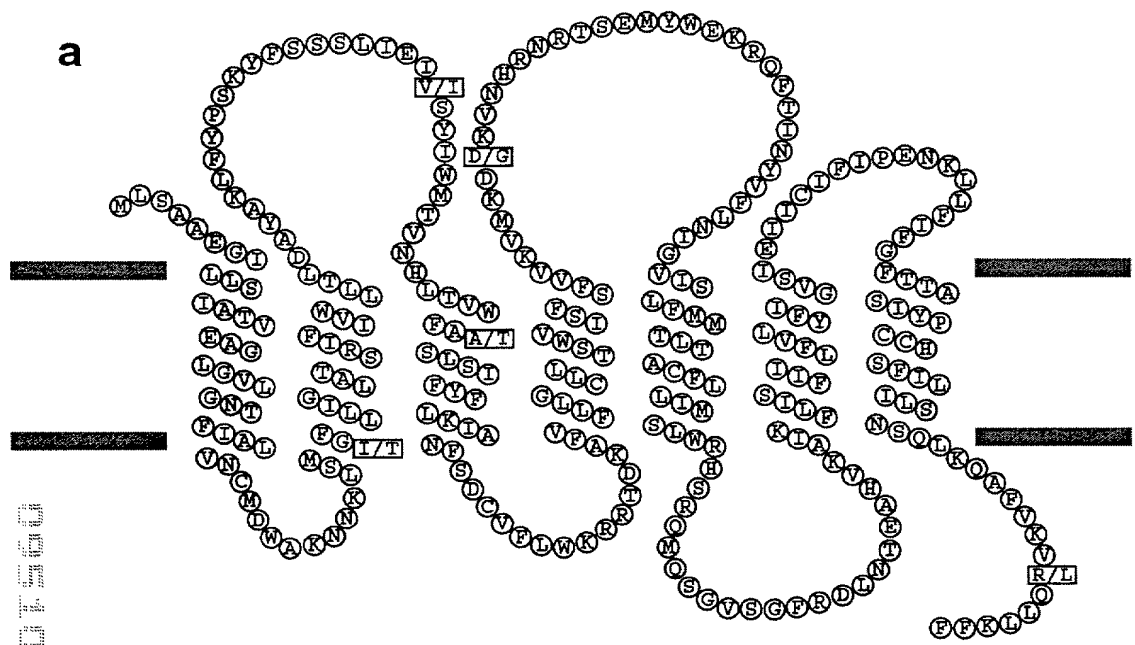
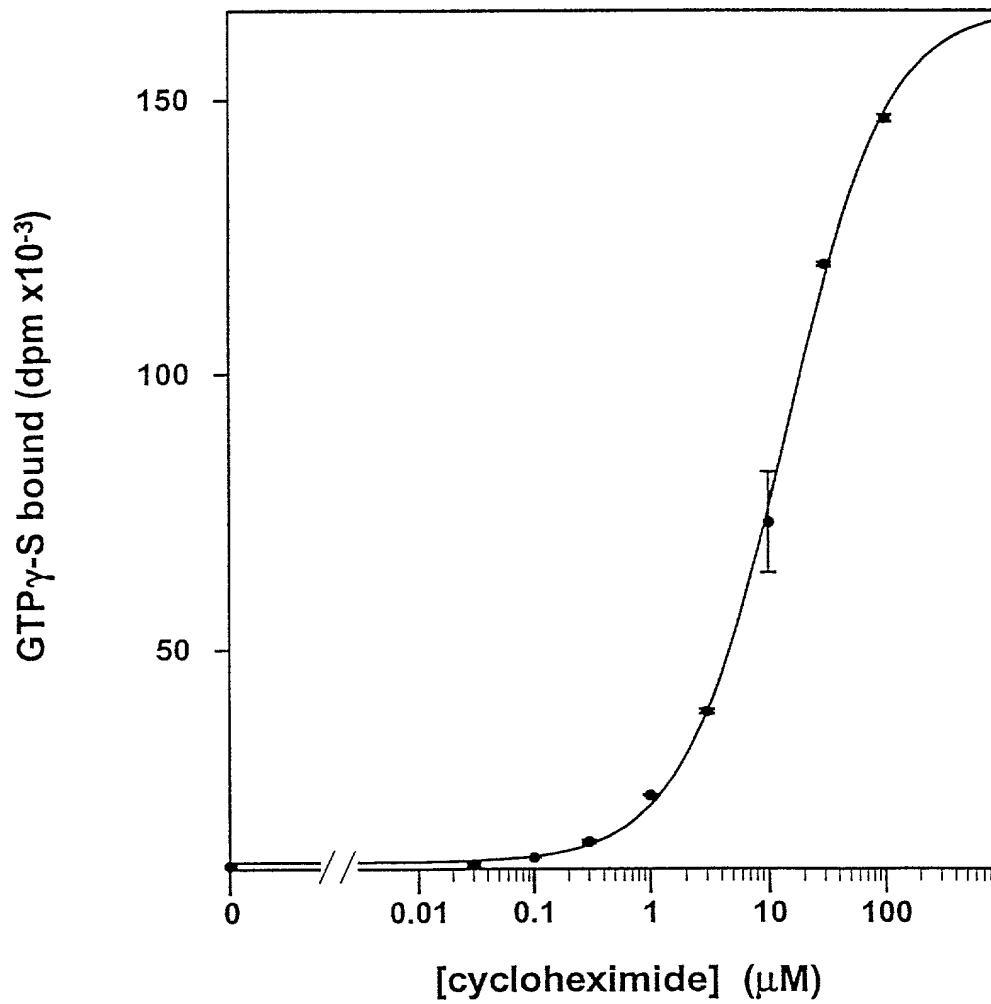
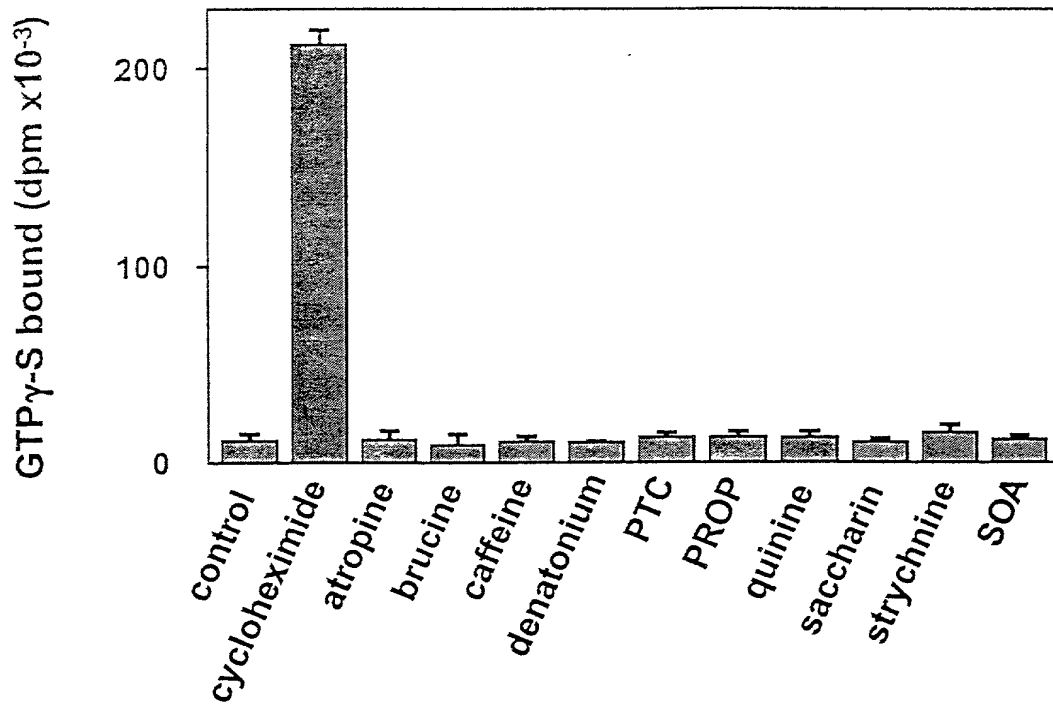


Figure 7



<p>ASGNLIEYISYFWVIGNQSSMWFEAT SLSIFYFLKIANFSNYIFLWLKSRT NMVLPFMIVFLLISSLLNFAYIAKI LNDYKTKNDTVWDLNMYKSEYFIKQ ILLNLGVIFFFFTLSLITCIFIILISL WRHNRQMOSNVTGLRDSNTEAHVKA MKVLISFIILFIFYFIGMAIEISCF TVRENKLLLMFGMTTITAIYPWGHF ILILGNSKLKQASLRVLQQLKCEK RKNLRVT</p>	<p>ACAGATATTCTCTCCAAATATATATGCCTCCGGTAACCTAATTGAATATA TTAGTTACTTTTGGGTAATTGGTAATCAATCAAGTATGTGGTTTGCCACC AGCCTCAGCATCTTCTATTTCTGAAGATAGCAAATTTTCCAACATACAT ATTTCTCTGGTTGAAGAGCAGAACAAATATGGTTCTTCCCTTCATGATAG TATTCTTACTTATTTTCATCGTTACTTAATTTTGCATACATTGCGAAGATT CTTAATGATTATAAAACGAAGAATGACACAGTCTGGGATCTCAACATGTA TAAAAGTGAATACTTTATTAAACAGATTTTGCTAAATCTGGGAGTCATTT TCTTCTTTACACTATCCCTAATTACATGTATTTTTTAATCATTTCCCTT TGGAGACACAACAGGCAGATGCAATCGAATGTGACAGGATTGAGAGACTC CAACACAGAAGCTCATGTGAAGGCAATGAAAGTTTGTATCTTTTCATCA TCCTCTTTATCTTGTATTTTATAGGCATGGCCATAGAAATATCATGTTTT ACTGTGCGAGAAAACAACTGCTGCTTATGTTTGAATGACAACCACAGC CATCTATCCCTGGGGTCACTCATTATCTTAATCTAGGAAACAGCAAGC TAAAGCAAGCCTCTTTGAGGGTACTGCAGCAATTGAAGTGCTGTGAGAAA AGGAAAAATCTCAGAGTCACATAG</p>
<p>>hGR11 aa MANMLKNMLTMISAIDFIMGIQSR VMVLVHCIDWIRRWKLSLIDFILTC WAISRIFXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXNHLCT*FATCL AVFYFLKIVNFSYLFYFWLKWINK VAFILPLVSASFVYQLSFDVHF*CL LVSCPKKYERHMTGLLNVSNNKNVN NIIFFIGSLSSFSISSIFFLLLLL SS*RHMKHIRENFRDCRTPVYGPIS EPRKRESFFVLLLYKNLPFS</p>	
<p>>hGR12 aa MSSIWETLFIRILVV*FIMGTVGN* FIVLVNIID*IRN*KVSLIDFILNC LAISRICFL*ITILATSFNIGYEKM PDSKNLAVSFDILWTGSSYFCLSCT TCLSVFYFLKIVANFSNPIFLWMKW IHKVLLEFIVLEATISFCTTSILKEI IINSLI*ERVTIKGNLTFNYMDTMH DFTSLFLLQMMFELPFVETLASILL LILSLWSHTRQMKLHGIYSRDPSTE AHVKPIKAIISFLLLFIVHYFISII LTLACPLLDFAARTFSSVLVFFHP SGHSFLLILRDSKLKQASLCVLKKM KYAKKDIISHFYKHA</p>	<p>>hGR12 nt ATGTCAAGCATTTGGGAGACACTGTTTATAAGAATTCTTGTAAGTGAATT CATAATGGGGACTGTGGGAAATTGATTCAATTGATTGGTTAATATCATTG ACTGAATCAGGAAGTAAAGGCTCTCCCTGATTGATTTTATTCTCAACTGC TTGGCCATCTCCAGGATATGTTTCTGTAGATAACAATTTTAGCTACCTC TTTCAATATAGGCTATGAGAAAATGCCTGATTCTAAGAATCTTGCAGTAA GTTTTGACATTCTCTGGACAGGATCCAGCTATTTCTGCCTGTCTGTACC ACTTGCCCTCAGTGCTCTTCTATTTTCTCAAGGTAGCCAACTTCTCCAATCC CATTTTCTCTGGATGAAATGGAAATTCACAAGGTGCTTCTCTTTATTG TACTAGAGGCAACGATCTCTTTCTGCACAACCTCCATTCTGAAGGAAATA ATAATTAATAGTTTAACTAAGAACGGGTAAACAATAAAAGGCAACTTGAC ATTTAATTATATGGATACCATGCATGATTTCACCTCTCTGTTTCTCCTTC AGATGATGTTTCATCCTTCCCTTTTGTGGAAACACTGGCTTCCATTCTTCTC TTAATCCTCTCCTTATGGAGCCACACCAGGCAGATGAAGCTACATGGGTAT TTATTCCAGGGATCCCAGCACAGAAGCCCATGTAAAACCTATAAAAGCTA TAATTTCAATTTCTACTCCTCTTTATTGTGCATTATTTTCATCAGTATCATA CTAACATTGGCCTGTCTCTTCTAGACTTCGTTGCGGCAAGGACTTTTAG TAGTGTGCTGGTATTTTCCATCCATCTGGCCATTCAATTTCTTAATTT TACGGGACAGCAAAGTGAAGCAAGCTTCTCTGTGTCTCTGAAGAAGATG AAGTATGCCAAAAAGGACATAATCTCTCATTTTTTATAAACATGCCTGA</p>
<p>>hGR13 aa MESALPSIFTLVIIAEFIIGNLSNG FIVLINCIDWVSKRELSSVDKLLII LAISRIGLIWEILVSWFLALHYLAI FVSGTGLRIMIFSWIVSNHFNWLWA TIFSIFYLLKIASFSSPAFLYLKWR VNKVILMILLGTLVFLFLNLIQINM HIKDWLDRIYERNNTWNFSMSDFETF SVSVKFTMTMFSLTPFTVAFISFLL LIFSLQKHLQKMQNLNYKGRDPRK VHTNALKIVISFLLFYASFLLCVLI SWISELYQNTVIYMLCETIGVFSPS</p>	<p>>hGR13 nt ATGGAAAGTGCCCTGCCGAGATCTTCACTCTTGTAATAATTGCAGAATT CATAATTGGGAATTTGAGCAATGGATTATAGTACTGATCAACTGCATTG ACTGGGTCAGTAAAAGAGAGCTGTCTCAGTCGATAAACTCCTCATTATC TTGGCAATCTCCAGAATTGGGCTGATCTGGGAAATATTAGTAAGTTGGTT TTAGCTCTGCATTATCTAGCCATATTTGTGTCTGGAACAGGATTAAGAA TTATGATTTTGTAGCTGGATAGTTTCTAATCACTTCAATCTCTGGCTTGCT ACAATCTTCAGCATCTTTTATTGTCTCAAAATAGCGAGTTTCTCTAGCCC TGCTTTTCTCTATTTGAAGTGAGAGTAAACAAAGTGATTCTGATGATAC TGCTAGGAACCTTGGTCTTCTTATTTTAAATCTGATACAAATAAACATG CATATAAAAGACTGGCTGGACCGATATGAAAGAAACACAACCTTGAATTT CAGTATGAGTGACTTTGAAACATTTTCACTGTCTCGGTCAAATTCATATGA CTATGTTCACTCTAACACCATTACTGTGGCCTTCATCTCTTTTCTCCTG</p>

	TTGTGTTTACCTCTTACTTTCTAACCATACTCATCACCATTATAGGTACT CTATTTGATAAGAGATGTTGGTTATGGGTCTGGGAAGCTTTGTCTATGC TTTCATCTTAATGCATTCCACTTCACTGATGCTGAGCAGCCCTACGTTGA AAAGGATTCTAAAGGGAAAGTGCTAG
>hGR17 aa MCSAXLLIILSILVVFAFVLGNVAN GFIALINVDWVKTKISSTDQIVT ALAFSRIGLLXTLIILLHWYATVFN SALYSLEVRIVPSNVSAIINHFSIW LATSLSIFYLFKIANFSNFIFLHLK KRIKSVLLVILLGSLVFLICNLAVV TMDDSVWTKFEFEGNVTWKIELRNAI HLSNMTITNHASKLHTVHSDSNIFS AVSLFSXTMLANFTLFILTLISFLL LVCSPPCKHLKMMQLHGKGSQDLSTK VHIKPLQTVISFRMLFAIYFLCIIT STWNPRTQQSNLVFLLYQTLAIMYP SFHSFILIMRSRKLKQTSLSVLCQV TCWVK	>hGR17 nt
>hGR18 aa MFVGINIFFLVVATRGLVLGMLGNG LIGLVNCIEWAKSWKVSSADFILTS LAIVRIIRLYLILFDSFIMVLSPHL YTIRKLVKLFITLWALINQLSI*FA TCLSIIFYLLKIANFSHSLFLWLKWR MNGMIVMLLILSLFLLIFDSLVEI FIDISLNIIDKSNLTLYLDESKTLY DKLSILKTLTSLTYVIPFLLTLTSL LLLFI SLVRHTKNLQNSLGSRDSS TEAHKRAMKMVIAFLLLFIINFIST LIGDWIFLEVENYQVMMFIMMILLA FPSGHSFIIILGNKLRQSSLRLW HLKFSLLKKAPLTS	>hGR18 nt ATGTTTCGTTGGAATTAATATTTTCTTTCTGGTGGTGGCAACAAGAGGACT TGTCTTAGGAATGCTGGGAAACGGGCTCATTGGACTGGTAAACTGCATTG AGTGGGCCAAGAGTTGGAAGGTCTCATCAGCTGATTTCATCCTCACCAGC TTGGCTATAGTCAGAATCATTGACTGTATTAATACTATTTGATTCATT TATAATGGTATTGTCCCTCATCTATATACCATCCGTAACTAGTAAAC TGTTTACTATTCTTTGGGCATTAATTAATCAGTTAAGTATCTAGTTTGCC ACCTGCCTAAGCATTTTCTACTTGCTTAAGATAGCCAATTTCTCCCACTC CCTTTTCTCTGGCTGAAGTGGAGAATGAACGGAATGATTGTTATGCTTC TTATATTGTCTTTGTTCTTACTGATTTTTGACAGTTTAGTGCTAGAAATA TTTATTGATATCTCACTCAATATAATAGATAAAAGTAATCTGACTTTATA TTTAGATGAAAGTAAACTCTCTATGATAAACTCTCTATTTAAAAACTC TTCTCAGCTTGACATACGTTATTCCTTTCTTCTGACTCTGACCTCTTTG CTCCTTTTATTATATCTTAGTGAGACACACCAAGAATTTGCAGCTCAA CTCTCTGGGCTCAAGGGACTCCAGCACAGAGGCCCATAAAGGGCCATGA AAATGGTGATAGCCTTCTCCTCCTTTTATTATTAACCTTTATTTCCACT TTAATAGGAGATTGGATCTTCTCTGAGGTAGAGAATTATCAGGTGATGAT GTTTATTATGATGATTTTACTTGCTTTCCCTCAGGCCACTCATTTATTA TAATTTTGGGAAACAACAAGCTAAGACAGAGCTCCTTGAGACTACTGTGG CATCTTAAATTCTCTCTGAAAAAAGCAAACCTTTAACTTCATAG
>hGR19 aa VTTLANLIPFTLSLICFLLLICSLC KHLKKMRLHSGKSQDPSTKVHIKAL QTVTSFLMLFAIYFLCIITSTWNL TQQSKLVLLCQTVAIMYPSFHSFI LIMGSRKLKQTFLSVLWQMT	>hGR19 nt CTGTAACTACTCTAGCAAACCT CATACCCTTTACTCTGAGCCTAATATGTT TTCTGCTGTTAATCTGTTCTCTTTGTAAACATCTCAAGAAGATGCGGCTCC ATAGCAAAGGATCTCAAGATCCAGCACCAAGGTCCATATAAAAGCTTTGC AAACTGTGACCTCCTTCTCATGTTATTTGCCATTTACTTTCTGTGTATAA TCACATCAACTTGAATCTTAGGACACAGCAGAGCAAACCTGTACTCCTGC TTTGCCAAACTGTTGCAATCATGTATCCTTCATTCCACTCATTCCTGA TTATGGGAAGTAGGAAGCTAAACAGACCTTTCTTTAGTTTGTGGCAGA TGACATGCTGAGTGAAAGAAGAGAAACCTCAACTCCATAGATTCACAAGG GGAGCATCGTGGGTCTCTAGCAGAAAAACAACTGATGGTGTCTGGAACAT TTTATAT
>hGR20 aa HLXRKAKSVVLVIVLGSFLFLVCQL VMKNYINVTWTECEGNVTWKIKLR NAMHLSNLTVMAMLANLIPFTLTVIS FLLLIYSLCKHLKKMQLHGKGSQDP STKIHICALQTVTSFLVLLAIYFLC LIIS	>hGR20 nt TTCATCACTTANA AGGAAGGCTAAGAGTGTAGT TTCTGGTGATAGTGTTG GGGTCTTTGTTCTTTTGGTTTGTCAACTTGTGATGAAAAACACGTATAT AAATGTGTGGACAGAAGAATGTGAAGGAAACGTAACCTGGAAGATCAAAC TGAGGAATGCAATGCACCTTTCCAACTTGACTGTAGCCATGTAGCAAAC TTGATACCATTCACTCTGACCGTGATATCTTTCTGCTGTTAATCTACTC TCTGTGTAACATCTGAAGAAGATGCAGCTCCATGGCAAAGGATCTCAAG ATCCCAGACCAAGATCCACATAAAAGCTCTGCAAACTGTGACCTCCTTC CTCGTATTACTTGCCATTTACTTTCT GTGTCTAATCATATCCTTTTG
>hGR21 aa MPPGIGNTFLIVMMGEFII*MLGNG	

bioRxiv preprint doi: <https://doi.org/10.1101/2020.03.10.288888>; this version posted March 10, 2020. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

<p>FIVLVNCIDW*GVK*SY*TTASSPA WLSQSVNFG*YYLIHL*QHYGHIY MPSIN**NLFIFFGH*PIT*LPGLL P*CFLLL*NTYFSPCFIWLWRIS RTLLELPLGSLLLLFFNLALTGGLS DLWINIYTIYERNSTWSLDVSKILY CSLWILVSLIYLIISFLLSLISLLLL ILSLMRHIRNLQLNTMGPRDLRMKA HKRAMKMKMMKMMVSFLLFFLVHFFS LLPTGWIFLIQK*QANFFVLLTSI IFPSSHVSFVILENCKLRQTAVGPL WHLKCHLKRVKL</p>	
<p>>hGR22 aa MATESDTNLLILAIIEFIISMLGNV FIGLVNCSEXIKNXKVSADFILTC LAISHNGQLLVILFDSFLVGLASHL YTTYRLXKNCIMLWT</p>	<p>>hGR22 nt TATAGGGACNGTGATGCTTCGTACACTCTCCAAGAAGAAACACTCCGTGAG GTATGTGAGACTGCATNCCTTAGTAGATCTNNTGGGATATATATTCATAAT ATAGAAAAANAGGCAAGACTTNCTTAAGTATATGAGACTCTATCCAACAG CAGAAGGTTCTGATCAAGACTGGAAGTGCAATANAAGCAATGAAGATAAGT ATCAGATATGAATGCTCTTCTGCAATGGTCTGATTGTNACATTATTAATGA TACANAGTATTA AAAACTTGGATTTTNTGTCTCTGGAGATGGCCACCGAA TCGGACACAAATCTTCTGATTCTGGCAATAGCAGAATTCATCATCAGCATG CTGGGGAATGTGTTCACTGGACTGGTAACTGCTCTGAANGGATCAAGAAC CANAAGGTTCTCTCAGCTGACTTCATCCTCACCTGCTTGGCTATCTCTCAC AATGGACAACCTGTTGGTGATACTGTTTGATTCACTTCTAGTGGGACTTGCT TCACATCTATATACCACATATAGACTANGAAAAAACTGTATTATGCTTTGG ACATGACTAATCACTTGACACACTGCTTCGCACGTCTAGCATATTCTATT CTTAGATAGCCACTTCNCACTCCTTGCTCTGCTGAAGTGGGAT</p>
<p>>hGR23 aa VAFVLGNVANGFIALVNVIDXVNTR KISSAEQILTALVVSRIQXTLXHSI P*DATRC*SALYRXEVRIVASN</p>	<p>>hGR23 nt AGGGTTGAGTCGTGCTTATCTTCACTTAACCTAGTATANAANTACAGCATA TAGCAAGGAGAGAATGTATATGAAGAGGAGTGAATTTGAGTCTGTTTGAGA ATAATGACCTTTTCTATTTCTATAAAGACAGTTTTGAATTCATCTATTAGC ATATGCTGGTGCTTGCTCTGTGACACTAGTCACTGAATTTAAAGGCAGAAA ATGTTATTGCACATTTAGTAATCAAGTGTTTCATCGAAGTTAACATCTGGAT GTTAAAGGACTCAGAACAAAGTGTTACTAAGCCTGCATTTTTTTTATCTGTTT AACATGATGTGTTNTCTGCTCATCATTTTCATCAATCTGGTAGAGTTGCA TTTGTTCTTGGAATGTNGCCAATGGCTTCATAGCTCTAGTAAATGTCTATT GACTGNGTTAACACACGAAAGATCTCCTCAGCTGAGCAAATTTCTCACTGCT CTGGTGGTCTCCAGAATTGGTNNTACTCTGNGTCACTAGTATTCTCTGAGAT GCAACTAGATGTTAATCTGCTCTATATAGGNTAGAAGTAAGAATTGTTGCT TCTAATGCCTGAGCTCGTACGAACCAT</p>
<p>>hGR24 aa MATELDKIFLILAIIEFIISMLGNV FIGLVNCSEGIKNQKVSADFILTC LAISTIGQLLVILFDSFLVGLASHL YTTYRLGKTVIMLWHMTNHLTTWLA TCLSIFYFFKIAHFPHSLFLWLRWR MNGMIVMLLILSLFLLIFDSLVLEI FIDISLNIIDKSNLTLYLDESKTLY DKLSILKTLLSLTSFIPFSLFTSL LFLFLSLVRHTRNLKSSLSGRDSS TEAHRAMKVMMSFLFLFIVHFFSL QVANGIFFMLWNNKYIKFVMLALNA FPSCHSFILILGNSKLRQTAVRLLW HLRNYTKTPNALPL</p>	<p>>hGR24 nt ATGGCCACCGAATTGGACAAAATCTTTCTGATTCTGGCAATAGCAGAATTC ATCATCAGCATGCTGGGGAATGTGTTTCATTGGACTGGTAAACTGCTCTGAA GGGATCAAGAACCAAAAGGTCTTCTCAGCTGACTTCATCCTCACCTGCTTG GCTATCTCCACAATTGGACAACCTGTTGGTGATACTGTTTGATTCACTTTCTA GTGGGACTTGCTTCACATTTATATACCACATATAGACTAGGAAAACTGTT ATTATGCTTTGGCACATGACTAATCACTTGACAACCTGGCTTGCCACCTGC CTAAGCATTTTCTATTTCTTTAAGATAGCCCACTTCCCCCACTCCCTTTTC CTCTGGCTGAGGTGGAGGATGAACGGAATGATTGTTATGCTTCTTATATTG TCTTTGTTCTTACTGATTTTGTGACAGTTTAGTGCTAGAAATATTATTGAT ATCTCACTCAATATAATAGATAAAAGTAATCTGACTTTATATTTAGATGAA AGTAAAACTCTCTATGATAAACTCTCTATTTTAAAACTCTTCTCAGCTTA ACCAGTTTTATCCCCTTTTCTCTGTTCTGACCTCCTTGCTTTTTTTTATTT CTGTCCTTGGTGAGACATACTAGAAATTTGAAGCTCAGTTCTTGGGCTCT AGAGACTCCAGCACAGAGGCCCATAGGAGGGCCATGAAAATGGTGATGTCT TTCCTTTTCTCTTCATAGTTCACTTTTTTTTCTTACAAGTGGCCAATGGG ATATTTTTTATGTTGTGGGAACAACAAGTACATAAAGTTGTCTAGTTAGCC TTAAATGCCTTTCCCTCGTGCCACTCACTTATTCTCATTCTGGGAAACAGC AAGCTGCGACAGACAGCTGTGAGGCTACTGTGGCATCTTAGGAACATATA AAAACACCAATGCTTTTACCTTTGTAG</p>

>hGR25 aa LSPFRMLFAIYFLCIITSTWNPERTQ QSNLVFLLYQTLAIMYPSFHSFIL MRSRKLKQTSLSVLCQVTCWVK	>hGR25 nt
>hGR26 aa MPPGIGNTFLIVMMGEFII*MLGNG FIVLVNCIDVRSQMILLDNCILTS AISTISQLWIIILLDSFVTALWPHLY AFNKLKFIHIFWALTNHLVTLWAC CLSVFYFFKIAFYFSHPCFIWLWRRI SRTLLELPLGSLLLLLFFNLALTGGL SDLWINIYTYERNSTWSLDVSKIL YCSLWILVSLIYLISFLLSLISLLL LILSLMRHIRNLQNTMGPRDLRMK AHKRAMKMKMKMMVSFLLFFLVHFS SLLPTGWIFLIQKK	>hGR26 nt
>hGR27 aa LANLIDWAENQICLMDFILSSLAIC RTLLLGCCVAIRCTYNDYPNIDAVN HNLIKIIITIFDILRLVSK*LGIWFA SYLSIFYLLKVALFHHAIFLWLKWR ISRAVFTFLMIFLFFYISIIISMIKI KLFLDQC*YKI*EKLLLEGRCE*SP PSC*PDAH*PGVVYSLYHFSYLMFL VCYLPKGKHCTAVVIGDWLQRPTE AYVRAMNIMIAFFFFHLLYSLGTSLS SVSYFLCKRKIVALGAYLSYPLSHS FILIMENNKVRKAL	
>hGR28 aa NICVLLIILSILVVSFAFVLGNVANG FIALINVNDW	>hGR28 nt
>hGR29 aa MQAALTAFFVLLFSLLSLLGIAANG FIVLVLGKEWL	>hGR29 nt
>hGR30 aa MITFLPIIFSILVVVTFVLGNFSNG FIALVNSIEWKTRKISSADQILTA LVVSRVGLLWVILLHWYANVENSAL YSSEVGAVASNISAIINHFSIWLAT SLSIFYLLKIANFNSNLI FLHLKKRI RSVVLVILLGPLVFLICNLAVITMD DSVWTKEYEGNVTWKIKLRNAIHLS NMTVSTLANLIPFILTLICFLLLIC SLCKHLKMKQLHGKGSQDPSTKVHI KALQTVTSFLLLCAIYFLSMIISVC NFRLEKQPVFMFCQAIIFSYPSTH PFILILGNKKLKQIFLSVLRHVRYW VKDRSLRLHRETRGALCVF	>hGR30 nt ATGATAACTTTTCTACCCATCATTTTTTCCATTCTGGTAGTGGTTACATTT GTTCTTGGAATTTTTCCAATGGCTTCATAGCTCTAGTAAATTCCATTGAG TGGGTCAAGACACGAAAGATCTCCTCAGCTGACCAAATCCTCACTGCTCTG GTGGTCTCCAGAGTTGGTTTACTCTGGGT CATATATTACATTGGTATGCA AATGTGTTAATT CAGCTTTATATAGTT CAGAAGTAGGAGCTGTTGCTTCT AATATCTCAGCAATAATCAACCATTTCAGCATCTGGCTTGCTACTAGCCTC AGCATATTTTATTTGCTCAAGATTGCCAATTTCTCCAACCTTATTTTTCTC CACTTAAGAAGAGAATTAGGAGTGTGTTCTGGTGATACTGTTGGGTCCC TTGGTATTTTGTATTTGTAATCTTGCTGTGATAACCATGGATGACAGTGTG TGGACAAAAGAATATGAAGGAAATGTGACTTGAAGATCAAATTGAGGAAT GCAATACACCTTTCAAATATGACTGTAAGCACACTAGCAAACCTCATACCC TTCATTCTGACCCTAATATGTTTTCTGCTGTTAATCTGTTCTCTGTGTAA CATCTCAAGAAGATGCAGCTCCATGGCAAAGGATCTCAAGATCCCAGCACC AAGGTCCACATAAAAGCTTTGCAAACGTGACCTCCTTTCTTCTGTTATGT GCCATTTACTTTCTGTCCATGATCATATCAGTTTGTAAATTTGGGAGGCTG GAAAAGCAACCTGTCTTCATGTTCTGCCAAGCTATTATATT CAGCTATCCT TCAACCCACCCATT CATCTGATTTTGGGAAACAAGAAGCTAAAGCAGATT TTTCTTTT CAGTTTGTGGCATGTGAGGTACTGGGTGAAAGACAGAAGCCTT CGTCTCCATAGATT CACAAGAGGGGCATTGTGTGTCTTCTAG
>hGR31 aa MTTFIPIIFSSVVVFLVIGNFANG FIALVNSIERVKRQKISFADQILTA	>hGR31 nt ATGACAACCTTTTATACCCATCATTTTTTCCAGTGTGGTAGTGGTTCTATT TGTTATTGGAATTTTGTCTAATGGCTTCATAGCATTGGTAAATTCCATTG AGCGGGTCAAGAGACAAAAGATCTCTTTTGCTGACCAGATTCTCACTGCT

LAVSRVGLLWVLLLNWYSTVFNPAP YSVEVRTTAYNVWAVTGHFSNWLAT SLSIFYLLKIANFNSNLI FLHLKRRV KSVILVMLLGPLLFLACQLFVINMK EIVRTKEFEGNMTWKIKLSAMYFS XMTVTIGAXLVPFTLSLISFLMLIC SLCKHLKKMQLHGEGSQDLSTKVHI KALQTLISFLLLCAIFFLFLIVSVW SPRRLRNDPVMVSKAVGNIYLAFD SFILIWRTRKKLKHFTLLILCQIRC	CTGGCGGTCTCCAGAGTTGGTTTGCTCTGGGTATTATTATTAAATTGGTA TTCAACTGTGTTTAAATCCAGCTTTTATAGTGTAGAAGTAAGAACTACTG CTTATAATGTCTGGGCAGTAACCGGCCATTTTCAGCAACTGGCTTGCTACT AGCCTCAGCATATTTTTATTGCTCAAGATTGCCAATTTCTCCAACCTTAT TTTTCTTCACTTAAAGAGGAGAGTTAAGAGTGTCTATTCTGGTGATGCTGT TGGGGCCTTTACTATTTTTGGCTTGTCAACTTTTTGTGATAAACATGAAA GAGATTGTACGGACAAAAGAATTTGAAGGAAACATGACTTGGAGATCAA ATTGAAGAGTGCAATGTACTTTTCANATATGACTGTAACCATTGGAGCAN ACTTAGTACCCTTTACTCTGTCCCTGATATCTTTTCTGATGCTAATCTGT TCTCTGTGTAAACATCTCAAGAAGATGCAGCTCCATGGAGAAGGATCGCA AGATCTCAGCACCAAGGTCCACATAAAAAGCTTTGCAAACTCTGATCTCCT TCCTCTTGTTATGTGCCATTTTCTTTCTATTCCTAATCGTTTCGGTTTGG AGTCCTAGGAGGCTGCGGAATGACCCGGTTGTCTGTTAGCAAGGCTGT TGGAACATATATCTTGCATTGACTCATTATCTAATTTGGAGAACCA AGAAGCTAAAACACACCTTTCTTTTGATTTTGTGTGAGATTAGGTGCTGA
>hGR32 aa HSFMLTMGSRKPKQTFLSAL	
>hGR33 aa MVYFLPIIFSILVVFAFVLGNFSNG FIALVNVIDWVKRQKISSADQILTA LVVSRVGLLWVILLHWYANVFNSAL YSLEVRIVASNISAVINHFSIWLA SLSIFYLLKIANFNSNLI FLHLKKRI KSVVLVILLGPLVFLICNLAVITMD ERVWTKEYEGNVTWKIKLRNAIHLS SLTVTTLANLIPFTLSLICFLLLIC SLCKHLKKMQLHSGSQDPSTKVHI KALQTVISFLMLCAIYFLSIMISVW NLRSLNKPVMFCKAIRFSYPSIH PFILIWGNKKLQTFLSVFWQVRYW VKGEKPSSP	>hGR33 nt ATGGTATATTTTTCTGCCCATCATTTTTTCCATTCTGGTAGTGTTTGCATT TGTTCTTGGAATTTTTCCAATGGCTTCATAGCTCTAGTAAATGTCATTG ACTGGGTAAAGAGACAAAAGATCTCCTCAGCTGACCAAATCTCACTGCT CTGGTGGTCTCCAGAGTTGGTTTACTCTGGGTCAATATTATTACATTGGTA TGCAAATGTGTTTAAATTCAGCTTTATATAGTTTAGAAGTAAGAATTGTTG CTTCTAATATCTCAGCAGTAATCAACCATTTTCAGCATCTGGCTTGCTGCT AGCCTCAGCATATTTTTATTGCTCAAGATTGCCAATTTCTCCAACCTTAT TTTTCTCCACCTAAAGAAGAGAATTAGAGTGTGTTCTGGTGATACTGT TGGGGCCTTGTTGATTTCTGATTGTGAATCTTGCTGTGATAACCATGGAT GAGAGAGTGTGGACAAAAGAATATGAAGGAAATGTGACTTGGAAAGATCAA ATTGAGGAATGCAATACACCTTTCAAGCTTGACTGTAACACTCTAGCAA ACCTCATACCCTTTACTCTGAGCCTAATATGTTTTCTGCTGTTAATCTGT TCTCTTTGTAAACATCTCAAGAAGATGCAGCTCCATAGCAAAGGATCTCA AGATCCCAGCACCAAGGTCCACATAAAAAGCTTTGCAAACTGTGATCTCCT TCCTCATGTTATGTGCCATTTACTTTCTGTCCATAATGATATCAGTTTGG AATCTTAGGAGTCTGGAACAAACCTGTCTTCATGTTCTGCAAGCTAT TAGATTAGCTATCCTTCAATCCACCATTCTCCTGATTTGGGGAACA AGAAGCTAAAGCAGACTTTTCTTTTCTGTTTGGCAAGTGAGGTACTGG GTGAAAGGAGAGAAGCCTTCATCTCCATAG
>hGR34 aa GSSRXKPPRI PHKKLCKLGPSPFHN NLPIYFLCXNHIVLEFLKMRPKKCC SLMLCQAFGIIYPSFHSFILXWGNK TLKQTFLSVXWQVTCWAKGQNQSTP	
>hGR35 aa NAIRPSKLWTVTEADKTSQPGTSANK FSAGNLISHVNMSRRMQLHGKGSQHL TRVHIKAXQTVISFLMLXAIYFLCLI STWNPRTOQSKLVFLLYQTLGFMYYL HSFILTMGSRKPKQTFLSAL	
>hGR36 aa MICFLLIILSILVVFAFVLGNFSNG FIALVNVIDWVKRQKISSADQILTA LVVSRVGLLWVILLHWYSNVLSAL YSSEVIFISNAWAIINHFSIWLAT SLSIFYLLKIVNFSRLIFHHLKRKA KSVVLVIVLGPLVFLVCHLVMKHTY INVWTKEYEGNVTWKIKLRNAIHLS NLTVSTLANLIPFTLTLSFLLLIY SLCKHLKKMQLHGKGSQDPSTKVHI	>hGR36 nt ATGATATGTTTTCTGCTCATCATTTTATCAATTCTGGTAGTGTTTGCATT TGTTCTTGGAATTTTTCCAATGGCTTCATAGCTCTAGTAAATGTCATTG ACTGGGTCAAGAGACAAAAGATCTCCTCAGCTGACCAAATCCTCACTGCT CTGGTGGTCTCCAGAGTTGGTTTACTCTGGGTAATATTATTACATTGGTA TTCAAATGTGTTGAATTAGCTTTATATAGTTTCAAGTAATAATTTTAA TTTCTAATGCCTGGGCAATAATCAACCATTTTCAGCATCTGGCTTGCTACT AGCCTCAGCATATTTTATTTTGTCTCAAGATCGTCAATTTCTCAGACTTAT TTTTCATCACTTAAAAAGGAAGGCTAAGAGTGTAGTTCTGGTGATAGTGT TGGGTCCCTTGTTATTTTTGGTTTGTACCTTGTGATGAAACACACGTAT ATAAATGTGTGGACAAAAGAATATGAAGGAAATGTGACTTGGAAAGATCAA

KALQTVTSFLLLC AIYFLSMIISVC NFRLEKQPVFMFCQAIIFSYPSTH PFILILGNKKLKQIFLSVFWQMRYW VKGEKPSSP	ACTGAGGAATGCAATACACCTTTCAAACCTTGACTGTAAGCACACTAGCAA ACTTGATACCTTCACTCTGACCCTGATATCTTTTCTGCTGTTAATCTAC TCTCTGTGTAACATCTCAAGAAGATGCAGCTCCATGGCAAAGGATCTCA AGATCCCAGCACCAAGGTCCACATAAAAGCTTTGCAAACCTGTGACCTCCT TTCTTCTGTTATGTGCCATTTACTTTCTGTCCATGATCATATCAGTTTGT AATTTTGGGAGGCTGGAAAAGCAACCTGTCTTCATGTTCTGCCAAGCTAT TATATTCAAGTATCCTTCAACCCACCCATTTCCTGATTTTGGGAAACA AGAAGCTAAAGCAGATTTTCTTTTCTGAGTTTGTGGCAAATGAGGTACTGG GTGAAAGGAGAGAAGCCTTCATCTCCATAG
>hGR37 aa MITFLPIIFSILIVVTFVIGNFANG FIALVNSIEWVKRQKISSADQISHC SGGVQNWFTLGHIITLVCNCV*FGF I*IRSKNFWF*CLSNNQAFQHVGV SLSIFHLLKTANFSLIFLHLKKRI KSVGLVILLGPLLFFICNLFINMD ESVWTKEYEGNVTWKIKLRSAMYHS NMTLTM LANFVPFTLTLISFLLLIC SLCKHLKMKQLHGKGSQDPSTKVHI KALQTVTSFLLLC AIYFLSMIISVC NFRLEKQPVFMFCQAIIFSYPSTH PFILILGNKKLKQIFLSVLRHVRYW VKGEKPSSS	>hGR37 nt ATGATAACTTTTCTGCCCATCATTTTTCATTCTAATAGTGGTTACATT TGTGATTGGAAATTTTGTCTAATGGCTTCATAGCTCTAGTAAATTCCATTG AGTGGGTTAAGAGACAAAAGATCTCATCAGCTGACCAAATTTCTCACTGC TCTGGTGGTGTCCAGAAATGGTTTACTCTGGGTCTATTATTACATTGGT ATGCAACTGTGTTTAAATTTGGCTTCATATAGATTAGAAGTAAGAATTTT GGTTCTAATGTCTCAGCAATAACCAAGCATTTCAGCATGTGGGTGTACT AGCCTCAGCATATTTTCATTGTGCTCAAGACTGCCAATTTCTCCAACCTTAT TTTTCTCCACCTAAAGAAGAGGATTAAGAGTGTGGTTTGGTGATACTAT TGGGGCCTTTGCTATTTTTCATTTGTAATCTTTTGTGATAAACATGGAT GAGAGTGTATGGACAAAAGATATGAAGGAAACGTGACTTGGAAAGATCAA ATTGAGGAGTGCAATGTACCATTCAAATATGACTCTAACCATGCTAGCAA ACTTTGTACCTTCACTCTGACCCTGATATCTTTTCTGCTGTTAATCTGT TCTCTGTGTAACATCTCAAGAAGATGCAGCTCCATGGCAAAGGATCTCA AGATCCCAGCACCAAGGTCCACATAAAAGCTTTGCAAACCTGTGACCTCCT TTCTTCTGTTATGTGCCATTTACTTTCTGTCCATGATCATATCAGTTTGT AATTTTGGGAGGCTGGAAAAGCAACCTGTCTTCATGTTCTGCCAAGCTAT TATATTCAAGTATCCTTCAACCCACCCATTTCCTGATTTTGGGAAACA AGAAGCTAAAGCAGATTTTCTTTTCTGAGTTTGTGGCATGTGAGGTACTGG GTGAAAGGAGAGAAGCCTTCATCTTCATAG
>hGR38 aa MLTLTRIRTVSYEVRSTFLFISVLE FAVGFLTNAFVFLVNFWDVVKRQPL SNSDCVLLCLSLISRLFLHGLLFLSA IQLTHFQKLSEPLNHSYQAIIMLWM IANQANLWLAACLSLLYCSKLIRFS HTFLICLASWSPGRSPVPS	>hGR38 nt
>hGR39 aa LRNAGLNDNAKLVRNNDLLLINLI LLLPLSVFVMCTSMFLVSLYKMHMW MQSESHKLSSARTEAHINALKTVT FFCFVSYFAAFMANMTFRIPYRSH QFFVVKIEMAAYPAGHSVIIIVLSNS KFKDLFRMICLQKE	>hGR39 nt
>hGR40 aa SQYSLGHSYVVIFGYGQMKKTF LGI LWHLKCGLKGRALLATQVGLREKST RSLGVIFLASSYSFFVYVLCH	>hGR40 nt
>hGR41 aa MITFLLIILSILVVFAFVLGNFSNG FIALVNVIDWVNTRKISSADQILTA LAVSRVGLLWVILLHWYANVLNPAL YSSEVIIIFISNISAIINHFSIWLAT SLSIFYLLKIVNFSRLIFHHLKRKA KSVVLVIVLGPLVFLVCHLVMKHTY INVWTKEYEGNVTWKIKLRNATHLS NLTVSTLANLIPFTLTLISFLLLIC SLCKHLKMKQLHSGKSQDPSTKVHI KALQTVTSFLLMLFAIYFLYLITSTW NL*TQQSKLVFMFCQTLGIMYPSFH	>hGR41 nt

SFILIMGSRKLKQTFLSVLCQVTCL VKGQQPSTP	
>hGR42 aa FIGLTD CIAWMRNQKLCMVGFILTR MALARINIL	
>hGR43 aa LELIFS*KVVATRGLVLGMLGNGLI GLVNCIEWAKSWKVSSADFILTSLA IVRIIRLYLILFDSFIMVLSPHLYT XXXXXXXXXXXXXXXXXXXXXXXXXSL SIFHWFKTANFNSNLIPLKEED*N VWLGDVAVGALGIFHL*SCSENHG*E VCGQKNMKEFCSGMIKLRNAIQLSN LTVTMPANVTPCTLTLSFLLLIYS PCKHVKKMQLHGKGSQHLSTKVHIK VLQTVISFFLLCAIYFVSVIISVWS FKNLENKPVFMFCQAIGFSCSSAHP FILTMGNKKLKQTYLSVLWQMR	
>hGR44 aa MITFLPIIFSILIVVIFVIGNFANG FIALVNSIEWVKRQKISFVDQILTA LAVSRVGLLWVLLLHWYATQLNPAF YSVEVRITAYNVWAVTNHFSSWLAT SLSMFYLLRIANFNSNLIPLRIKRRV KSVVLVILLGPLLFLVCHLFVINMD ETVWTKEYEGNVTWKIKLRSAMYHS NMTLTMLANFVPLTLTLISFLLLIC SLCKHLKKMQLHGKGSQDPSTKVHI KALQTVTSFLLLCIYFLSMIISVC NLGRLEKQPVFMFCQAIIIFSYPSTH PFILILGNKKLKQIFLSVLRHVRYW VKDRSLRLHRETRGALCVF	
>hGR45 aa MATELDKIFLILAI AEFIISMLGNV FIGLVNCSEGIKNQKVFSADFILTC LAISTIGQLLVILFDSFLVGLASHL YTTYRLGKTVIMLWHMTNHLTTWLA TCLSIFFYFFKIAHFPHSLFLWLRWR MNGMIVMLLILSLFLLIFDSLVLLEI FIDISLNIIDKSNLTLYLDESKTLY DKLSILKTLLSLTSFIPFSLFLTSL LFLFLSLVRHTRNLKLSSLGSRDSS TEAHRRAMKMVMSFLFLFIVHFFSL QVANWIFFMLWNNKCIKFVMLALNA FPSCHSFILILGNSKLQQTAVRLLW HLRNYTKTPNPLPL	
>hGR46 MSFLHIVFSILVVVAFILGNFANGF IALINFIWVKKQKISSADQIIADK QSPELVCSG	
>hGR47 aa MLNALYSILIIIIINI*FLIGILGNG FITLVNGIDWVKM*KRSSILTALTI SRICLISVIMVRWFI	
>hGR48 aa VSRVGLLWVILLHWYSTVLNPTSSN	

CATTCTCACAATTGTCAATTGCTTCACAAATTCAGATAAATCCCCCTTCCT
 GTCAGGAATGTATTGTCTGTGCATTCAATGCTCACCATGCTAAGCCATTCA
 TTCCCTTCCTAACTTGAGTTTAAGAAGAAAATGCTTACTGTTGCCCATGT
 CCTATTGTGCTGCTTCTGGATGTTTTATGCAGTGATTTAGACACACGCCCT
 TGCCTGTCTCCAAATACTGGCCCTTTATTCTTTTATAAGTCTAGTAGAAAA
 TGAACCTCGTCTTTACTTCATTGACGAAGACATTGTATTCTTCCCCAAAATA
 GTGTTTAACTACTCTAGTCTCATCCATAATATCCCTAAATATCAGTGATTT
 CAGTGAGTAAACCTGACAACAGTTATTGCTTTGACTCTTAATTCAATTGT
 GCTGTAACATAGAGGAAACATTCTAGAACATTTCCATATTAATTTGTGCTT
 GTAGCAAACCAAATTTCTCCCCAGTTGGGTAAAAATATCAAAGCACAGAG
 TAATCAATTTTGAAATCACTCAGAAGACATCATTGTTCTATATATGTTTTT
 TTTAACTTCCCTCTAACAAGTATCAGATCTTTCCTTTACAGGGTCTGGT
 CTTACCATGACTATATTTTATCACCATGACCTATTTCTCTTCTATCTCTTT
 GTTTTCACTAACTCAGTAGCAACCAAATATCACATTAATAGCTAACTCTGG
 GCACTTATTTCTCAGCCTTTATCTATCCAGACACTTTCAATGTATTTCTG
 CTAAACACAATGACATCTCTTTTTGTGTTCTAACGACAAGGAATCATAACT
 TTCCAACCTTTTATACATGGTAGACATATTTGGTGAACCTTAACCTCTGACTC
 TTTCTTTAGAACTGAACTACTCCGGAAGCAAGCCTTCTGATGGAGAA
 ATAGATACGGGTATCGTGATTCATTGTGAAAGTGAATCCGGTGCCTGGAA
 AGAAATGGATATTTTTTTTTCTCTTGAGTGTGTCACTCTGACATATGTTCC
 ATGTTGAATCCATATTTGATACTGATAGCATGAATGTAAGTAAAGCATGTA
 TGAAGTAAAGACTGCTACCAAACCTTCGATTCAACTTTCTCAGCAGTAT
 CCCTGATATTGCATAAGAAAGAAAAACACGCTGTCTACTTGAGAAGGA
 CGTGTTCCATGCAATGTGGATGTGTCCAGGCTACATTGGCTCAACTGCAG
 CTGAAGGTGGGATGGGAAATGGTATAGTTAGTAATGTCTGCTGAGCTGTCT
 CACTGGAAAGGATTCTGAGCAGAGTAAATGTAAGCAATGTGGCCAAGGTCT
 CTTAGGAATGGGTTGTAAGCTTGTAAGGAGTTGGGTTAGGATTTGGGA
 TCCTTTTCAAGATGGATTGAGCAAGAGCCACTGAACTTGACTATACCTTT
 GTTATTTGTATCTAAATCCAGAAGGGTCTTTCATGTTCCAAAATCTCAGA
 TAGCTGGAAGGAAGAAGGACTGTTCTCTTTACAAGTATATAAATAGAGAAT
 GAGCTAAAAAGGACCCCTCACCCCGCCGTCACACACAGGAATACTATTCT
 CAGAACTAGGGAGTATTTTAGTGTCTCACTATTTCCCTTTGAAAAAAG
 TGCAATGGAAAACCTATCCATGACATACATGAGGTTGGAGTGATAAAAAACA
 GCTGAAGGAAGAGGAAGTCTGAAAAAGATGGAACAGCAATGATGCTTGT
 CCTATATATGTGTGACACCCACTAGTTCCCAAGGAAACCTTACATCCATTA
 TCTCATTTCAAGCTGGAAGGACAAGTCAAGTCACTCAACCGACCCAGCTG
 GAAAAACAGACCTAAGAATGTTAACTCATACTGATGGTTATTTCTCACTCT
 AAAGTCAATGCAAAATGGATAGCAAACAAAGGGGCTATTTTTTTAAGGGACC
 AGAGGGTTTTCAATCTAGAATCAGAGAAAAGATAAAAAGGGAGATGCTATAG
 AAAACAATAGAGAAGATGTGGCCAAGAACAGGAAAATCTCCAGTTAGCT
 TGGCACTTAGGGGCAACATGTTTCTGTTGTTTCGTTCTCAATACTGTATT
 GCATGTTGGGCTCACTATGTTTTAGTTGTGAGTGGGTTGTGCTTCTGGAA
 TTAAGAAAGGTCTGTTTCTAGATTTTCAGGTACAAATGTTTGAAGCCCATT
 GGTAGCATCAGTGAAATTAGGAAAAAACTGTGAGCACTGCTGGCTGGACTT
 GGCAAAGTCATTCACTATTTACACATCAAATATTAGCAACTTGAAAGTAA
 ATCTTTGCTCATCATCCAGTGGCCCCATGATCCTGGTGAATGACTTGTA
 TACTGTGGAGACTGGCAACGACGGTGAATTCTAGTAACACTTACCATAGA
 ATCTGTTTATAATTAGACTCGCCAGATTTTAGTTGCTAGAGAACAACTCTT
 TCTCCTTTACCCACATTCTCTAGTAGGATGCATAGGTTCCGGAACCCC
 CATGGCATCGTTTGAATCCTCCTGGTAGTCAAGAGAGTCCAGTCAACAGTC
 TCCGAAACACCTGCCAAGTCTTAACCTCCCAACAGTCTACAGTGTAACCTC
 AGTGTGTTGCATGAGGTTTATGTATCTCCTTACCATTTCCTAAATGTCAATA
 CCCGTGCACAGGATATTTGCATAGGCTGCCTCCAAGCCTGGGAAACACTCT
 CCTCCTCGCATTTGCTGGGTTTACCTTTCCAATTCAGTGTGCCCTTTAAA
 AGGCACTGCTTTTCTAGGCCCACTATTGCTGCTCAGCATGAACATCA
 AATCTACCACAGGCTTTTGCCTCTCAGAATTATTCTTTCTTCTACTATGCA
 ATGTGGTATCCATGAGAACTTTGTCACATTGTCAAATTTCTACCTTTGTTTT
 AATGnGnGCCTTTGTAATAGnGACTATGCCAGAAATTAATATAGTAAG
 ATGGGTAACAACnCTTCAATnTGGAATTTATAATTAAATAAATATATGT
 AATATTATGACTTATTATAAnGTCAATCTACTGTACCCTACTCCTACTAGG
 AATGCAAGACAAATAGCAATGTGATCAGCATGTGCTCTTTCACAGATCA
 TATTGTGCATGTTGCTGATGATGCCACAGTGCATCTATCAGAATATCTCT
 GATCATTTTTTTTTTTTTGCTTTTGAGAAGCCCCGGTTGGTGTGGGATGC


```
>rGR09 aa
MLSAAEGILLSIATVEAGLGVLGNT
FIALVNCMDWAKNKKLSKIGFLLFG
LATSRIFIVWILILDAYAKLFFPGK
YLSKSLTEIISCIWMTVNHMTVWFA
TSLSIFYFLKIANFSHYIFLWLKVR
TDKVFAFLWLCLLISWAISSFSTKR
VMKSNPKNHGNRSTSGTHWEKREFTS
NYVLINIGVISLLIMTLTACFLLI
SLWKHSRQMQSNVSGFRDLNTEAHV
KAIKFLISFIILFIFYFIGVAVEII
CMFIPENKLLFIFGLTTASVYPCCH
SVILILTNSQLKQAFVKVLEGLKFS
ENGKDLRAT
```

>rGR09 nt

GGACACTGCAGCAGATCTGCTATAGAATAACAGATACAAACATAGCAACCT
GCAGAGATGCTCAGTGCGCAGCAGAAGGCATCCTTCTTTCCATTGCAACATGTT
GAAGCTGGGCTGGGAGTTTATAGGGAACACATTATCGCCCTGGTTAACTGC
ATGGATTGGGCCAAGAACAAGAAGCTCTCTAAGATTGGTTTCTCTCTCTTT
GGCTTAGCAACTTCCAGAATTTTTATTGTATGGATATTAATTTTAGACGCA
TATGCAAAGCTATTCTTTCCGGGGAAGTATTTGTCTAAGAGTCTGACTGAA
ATCATCTCTGTATATGGATGACTGTGAATCACATGACTGTCTGGTTTGCC
ACCAGCCTCAGCATCTTCTATTTCCTAAAAATAGCAAAATTTTCCCACAT
ATATTTCTCTGGTTAAAGCAGGAGAAGCTGATAAAGTATTGGCTTTCTCTTTG
TGGTGTTTATTAATTTTCATGGGCAATCTCCTTCTCATTCACTGTGAAAGTG
ATGAAGAGCAATCCAAAGAATCATGGAACAGGACCAGTGGGACACATTGG
GAGAAGAGAGAATTACAAGTAACATATGTTTTAATCAATATTGGAGTCATT
TCTCTCTTGATCATGAGCTTAACTAGCTCATGTTCTTGTATTAATTATTTCACTT
TGGAAACACAGCAGGCACAGTGCAGTCTAATGTTTTCAGGATTACAGAGATCTC
AACACTGAAGCTCATGTGAAAGCCATAAAATTTTTAATTTCAATTTATCATC
CTTTTCATCTGTACTTTATAGGTGTTGCAGTAGAATCATCTGCATGTTT
ATCCCAAGAAAAACAACCTGCTATTTATTTTGGTTTGACACAGCTGCATCGTG
TATCCCTGCTGTCACTGCTGACTTCTAATTTCTAACAAACAGCCAGCTGAAG
CAAGCCTTTGTAAAGGTACTGGAGGGATTAAAGTTCTCTGAGAACGGAAAA
GATCTCAGGGCCACATGAGTCTGGAACAGAAATGGGTAGTCTGGAATAAATT
GTAAGGAAGTTCGTAGAAGGTCTTTTTTCATTTGTACAGTGCTCTTACCTTGT
TTTTGAGGAGATGTAACCTTTTTTATTTTATTTTATCTATGTGTAATA
AGTGTGTGTGTGTGTGTGTGTGTTTATGTGTGTGTGTATATGTCTATGT
GTGTTTTAGGAGGTTTAAAGAGGAAGAGGGAATAGAGGTATGTTGGTGT
TTAACATGGATATTCACAGGCCAAGGAACTTGTCTCTCCTTTTACCTTAG
GGTAGTGTCTTTGTGGCTGTCACTCTGACAGTCTACACTAGTTGAACATAA
GAGCTTTTAGCCAGTTCATCTGTCTAAACCTCCCTTCTCATGGTAGCAGTG
TTCTGATTACAGAATTGCTGTGCATACAGCTTTTAAACAAGTTTCCCA
TAGACAGAATTTCATGTCAAACGGAATGCACAGCTGTCACTCTTACCCACCG
ATCTCTCTTGCCAGCCCATTCCTATTGACTTTAAACTGTAGTATTAAACTT
TACTGGAATCTTCTGCAACAGCTGTGACTATGTCTTGTGAATCACATGAT
ATGGTGAATTTTAATGCCATGTGAAAATTGTTTGTTCAGTTAGTTTCTCT
ACTCTGCCAAATCATCTCTTACACTTGGCAGAAAAAACCATCACTGTG

SLSTFLLLLIFSLWTLHQRMQQHVQG GRDARTTAHFKAQTVIAFFLLYSI FILSVLIQNEILLKKNLFVVVFCEVVY IAFPTFHSYILIVGDMKLRQACLPL CIIAAEIQTTLCRNFRSLKYFRLCC IF	GCTTATAAGTTTAGTCATATTTCTTTTCATATTTCTGATATTTCTATGACTTC AAGGATGACACAAGTCAGTAATAATGTTTGGATTATAGTCAATCATTTCAG TATCTGGCTTTCTACATGCCTCAGTGTCTTTATTTTCTCAAGATATCCAA TTTTTCTAACTCTTTTTTTCTTTTATCTAAAGTGAGAGTTGAAAAGTAGT TTCAGTTACACTGTTGGTGTCTTGTCTCCTCTGATTTTAAATATTTTATT AATTAACCTGGAAATTAGCATATGCATAAAGGAATGTCAAAGAAACATATC ATGCAGCTTCAGTTCTCATTACTATGCAAAGTGTCAAGGCAGGTGATAAG GCTTCACATTATTTTCTGTCTGTCCCCGTTGTTTTGTCCCTGTCAACTTT TCTCCTGCTCATCTTCTCCCTGTGGACACTTCACCAGAGGATGCAGCAGCA TGTTCAGGGAGGCAGAGATGCCAGAACCACGGCCCACTTCAAAGCCCTACA AACTGTGATTGCAATTTTCTCTACTATATTTCCATTTTATTCTGTCTGTCTT AATACAAATATGAATTTACTGAAGAAAAATCTTTTCGTTATTTTGTGAGG TTGTATATATAGCTTTTCCGACATTCCATTATATATTTCTGATTGTAGGAG ACATGAAGCTGAGACAGGCCTGCCTGCCTCTCTGTATTATCGCAGCTGAAA TTCAGACTACACTATGTAGAAATTTTAGATCACTAAAGTACTTTAGATTAT GTTGTATATTTCTAGACAAAAATTAAGTATGACAAATGTCTTTGTATTTT CATTTTAAATATCCTTTAATTTTGTACTGCATGAAATTGATTTCTGCTTGCA ATTATCACTGATTAAACTATTAATAATTTAACTAGTTGTATACAAGG
>mGR02 aa MESVLHNFATVLIYVEFIFGNLSNG FIVLSNFLDWVIKQKLSLIDKILLT LAISRITLIWEIYAWFKSLYDPSSF LIGIEFQIIYFSWVLSSHFSWLWAT TLVSFYLLRIANCSWQIFLYLKWRL KQLIVGMLLGSILVFLGNLMQSMLE ERFYQYGRNTSVNTMSNDLAMWTEL IFFNMAMFESVIPFTLALISFLLIF SLWKHLQKMQQLISRRHRDPSTKAHM NALRIMVSFLLLYTMHFLSLLISWI AQKHQSELADIIGMITELMYPVSHS CILILGNSKLKQTSLCMLRHLRCRL KGENITIAYSNQITSFCVFCVANKS MR	>mGR02 nt CAGCACAGTGAAAACTCATGGGCCACTTGGTCACCCAGGGACAGGCGACG CTGTTATATGCCAAGCTTTCTATGAACATGGAATCTGTCTTCAACAATTT GCCACTGTACTAATAATACGTGGAGTTTATTTTTGGGAATTTGAGCAATGGA TTCATAGTGTTGTCAAACCTTCTGGACTGGGTCAATTAACAAAAGCTTTCC TTAATAGATAAAATTTCTTACATTGGCAATTTCAAGAATCACTCTCATC TGGGAAATATATGCTTGGTTTAAAGTTTATATGATCCATCTTCTTTTTTA ATTGGAATAGAATTTCAAATTATTTATTTTAGCTGGGTCCTTTCTAGTCAC TTCAGCTCTTGGCTTGGCCACAACCTCTCAGCGTCTTTTATTACTTCGATA GCTAACTGCTCCTGGCAGATCTTTCTCTATTTGAAATGGAGACTTAAACAA CTGATTGTGGGGATGTTGCTGGGAAGCTTGGTGTCTTGTCTTGGAAATCTG ATGCAAAGCATGCTTGAAGAGAGGTTCTATCAATATGGAAGGAACACAAGT GTGAATACCATGAGCAATGACCTTGCAATGTGGACCGAGCTGATCTTTTTT AACATGGCTATGTTCTCTGTAATACCATTTACATTGGCCTTGATTTCTTTT CTCCTGCTAATCTTCTCTTGTGGAAACATCTCCAGAAGATGCAGCTCATT TCCAGAAGACACAGAGACCCTAGCACCAAGGCCACATGAATGCCTTGAGA ATTATGGTGTCTTCTCTTGTCTTATACCATGCAATTTCTGTCTCTTCTT ATATCATGATTGCTCAAAAGCATCAGAGTGAAGTGGCTGATTTATTGGGT ATGATAACTGAACTCATGTATCCTTCAGTCCATTTCATGTATCCTGATTCTA GGAAATTTCTAAATTAAGCAGACTTCTCTTTGTATGCTGAGGCATTTGAGA TGTAGGCTGAAAGGAGAGAATATCACAATTGCATATAGCAACCATAAAT AGCTTTTGTGTATTCTGTGTTGCAACAAATCTATGAGGTAGTTGTTCAAG GAATCCTTCTTGCTATTGTATCATGGAAGTCATATGGGGAGTCTGAA AGAGCTGTCTTCTGTAAGCAAGGTTTGTATACACTAGTGGGGCTGGGACAC CAACCAAGCACAAAACCTAGCTATAACCTATCCTGGCTGCAGGATATGCT GGAACAATGGTGGCTTGGAAATGTGGGACTGGCAAAGCAATAGCTAGTCT AACTTGAGGCCCATTTCCACAGCAGGAAGCTCATGCCACCTCTGCCTGGAT GGCCAGGAAGCAAAATCTTGATGGCCCCAAGACCTATGGTAAACTGAACAC TACTGGAAAAAGAAAGACTCGTGTAAATGATCTATCAAATATTTCTAATG ATATTCTGATAAACTCATATATTAGTCCCTGTCTTAATCATCATCACTGGG ACTCCTTCCCAGCACCTGATGGGAGCAGATAGAGATCTACATCCAAATAGT AAGTGTATCTTGGGGAACCTCACTTAAGAATAGAAGGAACAATTATGAGAG CCAGAGTGATCCAGAACACTAGGATCACAGAATCACTAAGCAGCATGCAT AGGGGTTAATGGAGACTGAAGTGGCAATCACAGAGCCTGCATAGGTCTACA CTAAGTCTCTGTGTATATACTGTGGCTGTTTAGCTTAGGAATTTTGTGAG ACTCCTAACAATGGATAAGGAATTC
>mGR03 aa MVLTIIRAILWVTLITIISLEFIIGI LGNVFIALVNIIDWVKRGKISAVDK TYMALAISRTAFLLSLITGFLVSL DPALLGMRTMVRLLTISWMVTNHFS VWFATCLSIFYFLKIANFNSIFLV LKWEAKKVSVTLVSVIILIMNII VINKFTDRLQVNTLQNCSTSNLTKD	>mGR03 nt CTTTAATAGCAGGGTGTGAATATTTAAATTTTCTTTCTGCAGCAACTACTG AGGGCTTCAGACTGCTGTATACAGGGCATGAAGCATCTGGATGAAGTTCAG CTGTGCTGCCTTTGACAACAATTTTTTGTGTATGTGTGGAGAACATAAACC ATTTTCATTAGTGAAATTTGGCTTTTGGGTGACATTGTCTATGATAGTTCTG AAAGTGATTATGTTAAGAAATCAGACACAGCCGTCTAGAGATTGATTAAAC ACATCTTTGGTAGTTTCAAGAAATTAGATCATCATGGTGTGACAAATAG GGCTATTTTATGGGTAACATTGATACTATTATAAGTCTGGAGTTTATCAT AGGAATTTTAGGAAATGTATTCATAGCTCTCGTGAACATCATAGACTGGGT

YGLFLFISTGFTLTPFAVSLTMFLL LIFSLWRHLKNMCHSATGSRDVSTV AHIKGLQTVVTFLLLYTAFVMSLLS ESLNINIQHNTNLLSHFLRSIGVAFP TGHSCVLILGNSKLRQASLSVILWL RYKYKHIEWGP	TAAAAGAGGAAAGATCTCTGCAGTGGATAAGACCTATATGGCCCTGGCCAT CTCCAGGACTGCTTTTTTATTGTCACTAATCACAGGGTTCTTGGTATCATT ATTGGACCCAGCTTTATTGGGAATGAGAACGATGGTAAGGCTCCTTACTAT TTCTGGATGGTGACCAATCATTTCACTGTCTGGTTTGAACATGCCTCAG TATCTTTTATTCTCAAGATAGCTAATTTCTCAAATCTATTTTCTTGT TCTCAAATGGGAAGCTAAAAAGTGGTATCAGTGACATTGGTGGTATCTGT GATAATCTTGATCATGAACATTATAGTCATAAACAATCACTGACAGACT TCAAGTAAACACACTCCAGAACTGTAGTACAAGTAACACTTTAAAGATTA TGGGCTCTTTTATTATTAGCACTGGGTTTACACTCACCCCATTCGCTGT GTCTTTGACAATGTTTCTTCTGCTCATCTTCTCCCTGTGGAGACATCTGAA GAATATGTGTACAGTGGCACAGGCTCCAGAGATGTGACGACAGTGGCCCA CATAAAAGGCTTGCAAACCTGTGGTAACCTTCTGTCTATATATGCTTTT TGTTATGTCACTTCTTTCAGAGTCTTTGAATATTAACATTCAACATACAAA TCTTCTTTCTCATTTTTTACGGAGTATAGGAGTAGCTTTTCCACAGGCCA CTCCTGTGTACTGATTCTTGGAACAGTAAGCTGAGGCAAGCCTCTCTTTC TGTGATATTGTGGCTGAGGTATAAGTACAAACATATAGAGAATTGGGGCCC CTAAATCATATCAGGGATCCTTTTCCACATTCTAGAAAAAATCAGTTAAT AAGAACAGGAATTTAGGAAGGAATCTGAAATTATGAATCTCATAGGCCATG AACCTTCAGACAAAGGATTCATTAGAGAGATAGAGAGAGAACATTGTTATC TGTAACCTGACAGGCAACACTGTAGATTATGAAAATAAATGTGAGTCTGTA ATGGAAAGCAAAACATGCTATATTTTATTAATTGGTTTTGGTTTAAGGTCG GGATA
>mGR04 aa MLSALESILLSVATSEAMLGVLGNT FIVLVNYTDWVRNKKLSKINFILTG LAISRIFTIWIITLDAYTKVFLLT LMPSSLHECMSYIWIINHLVWFS TSLGIFYFLKIANFISHYIFLWMKRR ADKVFVFLIVFLIITWLASFPLAVK VIKDVKIYQSNTSWLIHLEKSELLI NYVFANMGPISLFIVAIACFLITI SLWRHSRQMOSIGSGFRDLNTEAHM KAMKVLIAFIILFIFYLGIETL CLFLTNNKLLFIFGFTLSAMYPCCH SFILILTSRELKQDTRALQRLKCC ET	>mGR04 nt CTGCAGCAGGTAAATCACACCAGATCCAGCAGAAGCCTTCTTGGAAATTGG CAGAGATGCTGAGTGCAGTGGAAAGCATCCTCCTTTCTGTTGCCACTAGTG AAGCCATGCTGGGAGTTTTAGGGAACACATTTATTGTACTTGTAACTACA CAGACTGGGTGAGGAATAAGAACTCTCTAAGATTAACTTTATTCTCAGCTG GCTTAGCAATTTCCAGGATTTTACCATATGGATAATAACTTTAGATGCAT ATACAAAGGTTTTCTTCTGACTATGCTTATGCCGAGCAGTCTACATGAAT GCATGAGTTACATATGGGTAAATTATTAACCATCTGAGCGTTTGGTTTAGCA CCAGCCTCGGCATCTTTATTTTCTGAAGATAGCAAATTTTCCACTACA TATTTCTCTGGATGAAGAGAAGAGCTGATAAAGTTTTGTCTTTCTAATTG TATTCTTAATTATAACGTGGCTAGCTTCTTTCCGCTAGCTGTGAAGGTCA TTAAAGATGTTAAATATATCAGAGCAACACATCCTGGCTGATCCACCTGG AGAAGAGTGAGTTACTTATAAACTATGTTTTTGCCAATATGGGGCCCATTT CCCTCTTTATTGTAGCCATAATTGCTTGTCTTGTGTTAACCATTTCCTTT GGAGACACAGCAGGCGAGATGCAATCCATTGGATCAGGATTAGAGATCTCA ACACAGAAGCTCACATGAAAGCCATGAAAGTTTTAATTGCATTTATCATCC TCTTTATCTTATATTTTTTGGGTATTCTCATAGAAACATTATGCTTGTTC TTACAAACAATAAATCTCTCTTATTTTTTGGCTTCACTTTGTGAGCCATGT ATCCCTGTTGCCATTCCTTTATCCTAATTCTAACAAGCAGGGAGCTGAAGC AAGACACTATGAGGGCATGCGAGAGATTAAATGCTGTGAGACTTGACAGA GAAATGAATGTTCTGGCACAGTTCAGCAGGGAATCCCTGGAGCCCTTTCCA TTCCCACTATGTTCTCACACTGTCTTTAGTTGAATTGTTAAAGTTTTTGA AACCTTTGGCAACTGATTGACTGCAGCTACGCCAGTGTAAAGATTTTCATAG TAAGAGCAAACATTGAAAATAAGACTTCTCAGTCTTATTTTATTGAGTTTC TAAAGCATTGACCCCATTCACCAGAAAAACCAAGGGGAAGAGAGGAGTT TTCAGACATGTGTGATGAATCTTGATATTTAGGACATGGAATTGAGGAG~C CAGAGGGATGCTACCGTGTGTCTACAGCTTTGTTTGTAAATAGCTACTTT TCCTTTCCAGTTAGTTAAAGTAGATGCTTGGAGTAGTGGTGAAATCATG GCAGTAGATGGGATCTGTGGGAAGTGGTTGAGGAAGCAGGCTGTTTCTGAA CGAAGAGACCAGAGGACTGATTGAACTGGTCATTGTGTATATCAAAATAG TGATTTGAGATGAAGCCAAGTTGTAGAGCAAAGATATCTGAGGAAGAATTC
>mGR05 aa MLSAAEGILLSIATVEAGLGVLGNT FIALVNCMDWAKNNKLSMTGFLIG LATSRIFIVWLLTLDAYAKLFYPSK YFSSSLIEIISYIWMVTNHLTVWFA TSLSIFYFLKIANFSDCVFLWLKRR TDKAFVFLGCLLTWSVISFSFVVK VMKDGKVNHRNRTSEMYWEKRQFTI NYVFLNIGVISLFMMTLTACFLIM	>mGR05 nt ATGCTGAGTGCAGGAGGATCCTCCTTTCCATTGCAACTGTTGAAGCT GGGCTGGGAGTTTTAGGGAACACATTTATTGCACTGGTAACTGCATGGAC TGGGCCAAGAACAATAAGCTTTCTATGACTGGCTTCTTCTCATCGGCTTA GCAACTTCCAGGATTTTTATTGTGTGGCTATTAACCTTTAGATGCATATGCA AAGCTATTCTATCCAAGTAAGTATTTTTCTAGTAGTCTGATTGAAATCATC TCTTATATATGGATGACTGTGAATCACCTGACTGTCTGGTTTGCACCAGC CTAAGCATCTTCTATTTCTTCTGAAGATAGCCAATTTTTCCGACTGTGATTT CTCTGGTTGAAGAGGAGAAGTATAAAGCTTTTGTTTTTCTCTTGGGGTGT TTGCTAACTTCATGGTAATCTCCTTCTCATTTGTTGTGAAGGTGATGAAG

	GGTGCAGATGAAACACTACAGCAGCAGCAACTCCAGCCTGAAAGCTCAGTT CACTGTTCTGAAGTCTCTTGCTACCTTCTTCACCTTCTTCACATCCTATTT TCTGACTATAGTCATCTCCTTTATTGGCACTGTGTTTGATAAGAAATCTTG GTTCTGGGTCTGCGAAGCTGTCATCTATGGTTTAGTCTGTATTCACTTCAC TTCAGTATGATGAGCAACCCTGCATTGAAAAAGGCACTGAAGCTCGAGTT CTGGAGCCCAGAGCCTTCTTGAGGCAGGAAACACAGTTAAGCCTCTAGGGT AAGGAGACTTTGCATTGGCACAGTCCCTATAGTGTAATGCAAACTTGAACA CAAACCTTCATCCCTTTTCACATCCACAAATGGCTGCATCTATACATCATCA CCAGTCTTCCCTGTATTCTGACCCATTCTTCTTCTGTCTATCCATAGTCC CCAGGTTGGTTTTGATTTTTCTCATGATCACACCAACTCTGCTTAGCTTTT GCCACCACTGTAATAGTAAACATGGGGTGTCTATATATTACAGTCAAAAT CATTCTCACATGTTGATTGCCTCACAAATTCATATAAATCCCCCTTCTTG TCAGGAATTTATTGTCTGCTCACTTAATGCTCACCATATATTAAGCCATT AATTCCCCCTTCTACCTTGAGTTTAAAGAGGAAATGTCTTACCATTGCC CACAACTATTCTGCTGCTTCTAGACTTTTATGCAAGTGATTTATACACAC ACACACACACACACACATACAAACAAC
>mGR19 aa MMEGHMLFFLLVVVVQFLTGVLANG LIVVVNAIDLIMWKMAPLDLLFC LATSRIILQLCILFAQLGLSCLVRH TLFADNVTIFYIINELSLWFATWLG VFYCAKIATIPHPLFLWLKMRISRL VPWLILASVVYVTVTTFIHSRETSE LPKQIFISFFSKNTTRVRPAHATLL SVFVFGTLPLFLIFTVAVLLLLSSL WNHSRQMRMTMVGTRPSRHALVSAM LSILSFLILYLSDHMAVLICTOGL HFGSRTFAFCLLVIGMPSLSHIVL ILGNPKLKRNAKTFIVHCKCCHCAR AWVTSRNPRLSDLPVPATHHSANKT SCSEACIMPS	>mGR19 nt CTGCAGCCTAGAGAACTAATGCATAGGAACTTATATTTCCACCTCCGTGA CGTCACTCTGACAGAAGTGAACCTTATATTTCCACCTCCGTGACGTCACTCT GACAGAAGTGACTTGTTTTGTATGATGCTCCAGGATGCCTCATTAGCATT GAGGACAATCATAATTAAGTAAGGCAAGGCATGAAGTGGTCCCTCACTAGG TACCTGGAGGCTTCTGGTTGCATGATTACTTGTGATGACTCTGACACTTA AGAAGACCTGAAAAATGCAAAGCTGTGATAAGGCACAGTTCTGTTTCTATG GTATCTCTTCTTATTTGACTGACATTGAGTTGAGAAGGCAGCACTATAAA CAAATGGGCCCCACCTTCTCTTCCATTGTCTTTGGGTGGGCATCATCTCC AAAGGAACCTTGGTCTAGTTGAAAGAAGCCAGAAATCATACATGGCTGAGA CTGTGCATAACTCTATGTATCATTTAAAGAAGTCATTGGTTCTTCTTATTT TAAATGATGGAAGGTCATATGCTCTTCTTCTTCTGGTCTGGTGTAGTGA GTTTTTAAGTGGGTCTTGGCAAATGGCCTCATTGTGGTTGTCAATGCCAT CGACTTGATCATGTGGAAGAAAATGGCCCCACTGGATCTGCTTCTTTTTTG CCTGGCGACTTCTCGGATCATTCTTCAATTGTGTATATTGTTTGCACAGCT GGGTCTATCCTGTTTGGTGAGACACACGTTATTTGCTGACAATGTTACCTT TGTCTACATTATAAACGAAGTCTGAGTCTCTGGTTTGGCCACATGGCTTGGTGT TTTCTACTGTGCAAGATTGCTACCATCCCTCACCCACTCTTTCTGTGGCT GAAGATGAGGATATCCAGTTGGTGCCATGGCTGATCCTGGCATCTGTGGT CTATGTAAGTGTACTACTTTTCATCCATAGCAGAGAGACTTCAGAACTTCC TAAGCAAATCTTTATAAGCTTTTTTTCTAAAAATACAACTCGGTCAGACC AGCGCATGCCACACTACTCTCAGTCTTTGTCTTTGGGCTCACACTACCATT TCTCATCTTCACTGTTGCTGTTCTGCTCTGTTGTCTCCCTGTGGAACCA CAGCCGGCAGATGAGGACTATGGTGGGAAGTAGGGAACCTAGCAGACATGC CCTCGTCAGTGCGATGCTCTCCATTCTGTCACTTCCCTCATCTCTATCTCTC CCATGACATGGTAGCTGTTCTGATCTGTACCCAGGCTCCACTTTGGAAG CAGAACCTTTGCATTCTGCTTATTGGTTATTGGTATGTACCCCTCCTTACA CTCGATTGTCTTAATTTTAGGAAACCCTAAGCTGAAACGAAATGCAAAAAC GTTCAATTGTCCATTGTAAGTGTGTGTCATTGTGCAAGAGCTTGGGTCACTC AAGGAACCCAGACTCAGCGACTTGCCAGTGCCTGCTACTCATCACTCAGC CAACAAGACATCCTGCTCAGAAGCCTGTATAATGCCATCTTAATTGTCCAA CCTGAGGCTTAATCATTTCAAAGGGTAAATTGATGATCAAAGCCCAACACA TGATATGACATCAAGGTCCATATCCAGTAGTCATGTGGAATACCACCTT GCAAAATGATGTCATTGAGAAACCAGGGCAAATGGAGTCTAGGTCTTTTCAG TATGATTTGCTGCAG
>mGR20 aa MNLVEWIVTIIIMTEFLLGNCANVF ITIVNFIDCVKRRKISSADRIITAI AIFRIGLLWAMLTNWHSHVFTPDTD NLQMRVFGGITWAITNHFTTWLGTI LSMFYLFKIANFNSFLHLKRKLD NVLLVIFLGSSFLVAYLGMVNIKK IAWMSIHEGNVTTKSKLKHVTSITN MLLFSLINIVPFGISLNCVLLLIYS LSKHLKNMKFYGKGCQDQSTMVHIK ALQTVVSFLLLYATYSSCVIISGWS	>mGR20 nt CTAGATGGGCTGTTTCATATAATGACTGGAACCTCCCTACATGCTCCACGTC TTGAGTTCTAAATTTCACTAACAAATTTTGACTGCCATAAATAATGAAG GTTTAAAGAAAGAACAACATTTGAAGCAATGGACCAGAATTCCTCTTTATT TGACTCTTAGCAAATTTGGAATGCAGCATCCTTTCAAGAGCAGCACTGAAAT ATACCAGTCAATGGCAGAGAGTAAAAAGTATGCAATTGGAGACATTATGG TAATATAAATTTCCATTAAAAATGAGACTGCATTACCTATTACAACACAT TGCTATTCTGCTCAACACAGAGTTAAAAAGAAACAAGAACTCTGTATACA TTCAGTTAGTCACAAGTATAATTATGTTACATATTTAAAAAATGAATC ATGATCTGTGAATTTAGCCTGGCTTTTTTTGTCTCTCTCTTTTATTTCTTT TCCTTTAGACAGACACAATGAATTTGGTAGAATGGATTGTTACCATCATAA TGATGACAGAAATTTCTCTTAGGAACTGTGCCAATGTCTTCATAACCATAG

TWLSVLFCIKIANFSPAFWLWKWR
 FPALVPWFLLGSILVSVIVTLLFFW
 GNHTIYQAFLLRRKFTGNTTFKEWNR
 RLEIDYFMPLKVVMTSIPCSLFLVS
 ILLLISSLRRLSRMQHNTHSLQDP
 NVQHSRALKSLISFLVLYAVSFVS
 MIIDATVFISSDNVWYWPWQIILYF
 CMSVHPFILITNNLRFRTFRQLLL
 LARGFWVA

CCTTGTACACATAAAAGTAATTGAAAAAGTAACTCTCTGAGATGACAGAT
 ACGTTAAATGGTTTTACTTTTTCAACCTGCTCCAGTAGGGGTCCCTTTAAT
 GTTTGTGCTAGTAGATGGGGGACTCTCAAGTATCTTTGTGGTAGACAAATC
 TAAGGTGGCCTTCATGAATACCAACCCAGACTTTTGTGACTTTGTGATCCC
 CCACCTTTGAAGTGGATAAGAGCTGTGACTTGAGTCTAATCAAAGGAGTCC
 AACGTGTGTTTTATTCTGTAACAGTGCCTTTGTGTTTCTAGTTAATAACACA
 GGCAAAGAAGGCTAGGGTGACATTCTAGGATTGTGTTATTTCTATCTTGC
 TCATGCCTCCCTCTGCTGGTCTAATGAAATAAGTCAGTGGCCATATTTAA
 TATGACTACGTGGCAAATACTGATGATAGCCTGTGTGTTCCAACAAATATC
 CAGTAGGAGACCTAGGCATTACAGTCTGCAGCCACAAGGAAATAGGTTCTT
 TCACTGGAAAAAGAGCAGTTTAGATGGTTATAAATTACTTAATCCATAGAA
 GCCATAGGGGCTTTATGTAGAGATTTGGGTAGAGAGGTAGACCTAGATATT
 GACTTAGGAGTGGCTATTCTGAGTGGGGGTAGATATATGGCAGGGAACT
 CAGATAAGAAAGACTTCTTTAGTGTACGATTTTCTAGGTATCTCCTTG
 TGCCAGATATCTATGCGTCTATGTACCTACCTACCTACCTACCTACCTACC
 TACCTACCTACCTACTGACACCTAATAGGAAGAGGCAAGTGGTCAACACCT
 GCAATGATGGGATAAGAATGATGGAACCTCAGTTACCAAGATTAAATACCT
 TCCCCACTGATGTTATTGCAAGCATGGCAGCATGTAGGCAAAATCAGAGAA
 GGCAAATCATGAGCAGCTGCTGCCCATGGTACCCGAGCCCGGGAAATATT
 TGCATCATATCTGAGCCAAAAGCACACCTTTTATCTACTGCTGAGCATTT
 TTCACATTGAAGTTCTGGCTCACATGCAGAATCCAACCATTTATCTCCTGT
 CTCAGAAAGGGAGTGTGAGGACTGTGGGTAGGGGAGGGGAGGAGGCCAGG
 AACCAAGGCAATCAGTGGTGACAGGAGGAGGGACTGAAATGCTACCAACAT
 TATCAGTTTTCTTTCATGTTGACCTTTGTTCTGCTCTGTTTCTGGGGATCC
 TGGCCAACGGCTTCATTGTGCTGATGCTGAGCAGGGAATGGCTACTGCGTG
 GTAGGCTGCTCCCTCGGACATGATCCTCTTCAGTTTGGGCACCTCCCGAT
 TCTTCCAGCAGTGTGTGGGATTGGTCAACAGTTTCTATTACTTCTCCTCATC
 TGGTTGAGTACTCCGGGAGCCTTGCCCGGCAGCTCATTAGTCTTCACTGGG
 ACTTCTGAACTCAGCCACTTTCTGGTTTTGTACCTGGCTCAGCGTCTCTGT
 TCTGTATCAAGATTGCTAATCTCTCCCATCTGCCTTCTGTGGTTGAAGT
 GGAGATTCCAGCGTTGGTGCCCTGGTTCTTGTGGGCTCTATCTTGGTGT
 CCGTCAATTGTAACCTGCTGTTCTTTTGGGGAACACACATATATACAGG
 CATTCTTAAGGAGAAAGTTTACTGGGAACACAACCTTTAAGGAGTGAACA
 GAAGGCTGGAAATAGACTATTTTCATGCCTCTGAAAGTTGTCAACCATGTCAA
 TTCCTTGTCTCTTTTCTGGTCTCAATTTTGTCTGTTGATCAGTTCTCTCA
 GAAGGCATTGCTAAGAATGCAGCACAAATACCCACAGCTTGAAGACCCCA
 ACGTCCAGGCTCACAGCAGAGCCCTGAAGTCACTCATCTCATTCTCGGTTCT
 TTTATGCGGTGTCTTTGTGTCCATGATCATTGATGCTACAGTCTTCATCT
 CCTCAGATAATGTGTGGTATTGGCCCTGGCAAATTATACTTTACTTTTGCA
 TGTCTGTACATCCATTATCCTCATCACCAATAATCTCAGTTCCGCGGCA
 CCTTCAGGCAGCTACTCCTGTTGGCCAGGGGATTCTGGTGGCCCTAGAAGG
 CTTGGTCTCTTTATCTAGAGCCTTTGAAGAGACTCAGGTGAGGGTAACCTC
 ACTTGAAGTGAGCTCATCTACGTGGAATGTCTTTGTAGGCAGGCATGGG
 GTCATACTGTGAGGTTCTCATTGGGAAAGAGGAGAAGAAAATACAGAGTG
 TCCTTCCTTACCTTAGGATATTATGAAAGTGGAAATCCGAATCCTGGACC
 AGTATTGATCTAAGTGCAAAGTACAATATGTCTGTTTCTTTCATGTCTGT
 TTTCTTTTGTACTGATTCATTCTCTAGGGAATAGTCTTGATCAACTGAA
 TCATCTCATCTGGCTGGCCACTGGGGAGGTAAAAGAACTTTGTGTCACTGC
 TGCATTGGGATATACATGGGTGGGAAGCAAGTGTCCCTGAGGCAGAGTAGC
 ACTCAGTATGAGAACCTCAAAGAGCAGGTGGCTGTGCATGCAGGGGCTGGG
 GCAAGGAGTCTGATCACTCTTCACTGTATGGGGATTATTTGTCTCTTGCC
 AAAATTTGGAGACTTTGGCTTTAGTTTTGTGAAGATGACTGGAAAAATTCT
 TAATGCTACCCTGTATCATTTCTCAATAATATTTCTCTTTCTGCCTTTA
 ATTTCTCCTATCTGCAGCGCCCTTGCTTGTATCCGTAATAAATAAAT
 AAATAAATAAATAAGCCCAATCCTCATTTTCTGTCTTTGGGAACCTTTT
 ACTTCCCAGGTATACGCTACAAAGCCACTTCTGCATTGAATAAACATTAT
 CTTTCATTGAGAAAAAGACTTAAGAATCTCACCTTTACAAAAAATAAATA
 AAAGAATCTCACTTATTTTATATTCAAATTCATTTTAAAAAGAAAAGCA
 CAGCATTAAATTTTCTAAATACTGTTTATAAATAAATTTGCTCTAAGAAT
 TATACAAATGTTTGAAGGTAACCTTTGGAAAAAAGTGTGATTAGACATG
 GATGTTTGTAAAGACAGAACAAGAGCTCTTGAAGTCCATGGCAGCTCATT
 GGTCTTGCCTTCAGTAGAGCTGTCTGAATCCTGTAACTCTTATGCCCTT
 TTGTAGCTTTTCTGCAGATC

<p>>mGR27 aa</p>	<p>>mGR27 nt</p> <p>GAATTCGCCCTTGC GGATCCGGGAACGGATT CATAGCACTGGTAAACTTC ATGGGCTGGATGAAGAATAGGAAGATTGCCTCCATTGATTTAATCCTCACA AGTCTGGCCATATCCAGAATTGTCTATTGTGCGTAATACTATTAGATTGT TTTATATTGGTGTATATCCAGATGTCTATGCCACTGGTAAAGAAATGAGA ATCATTGACTTCTCTGGACACTAACCAATCACTTAAGTATCTGGTTTGCA ACCTGCCTCAGCATTTACTATTCTTCAAGATAGGTAATTTCTTTACCCA CTTTTCTATGCCTCAAGTCTAGACGCCAAGGGC</p>
<p>>mGR28 aa</p> <p>GREWLRYGRLPLDMILISLGASRF CLQLVGTVHNFFYSAQKVEYSGGLG RQFFHLHWHFNLNSATFWFCSWLSVL FCVKIAN</p>	<p>>mGR28 nt</p> <p>GAATTCGCCCTTGC GGATCCGGGAACGGGTTTATTGTGCTGGTGCTGGGGC AGGGAGTGGCTGCGATATGGCAGGTTGCTGCCCTTGGATATGATCCTCATT AGCTTGGGTGCCCTCCCGCTTCTGCCTGCAGTTGGTTGGGACGGTGACACAC TTCTACTACTCTGCCCAGAAGGTCGAGTACTCTGGGGGTCTCGGCCGACAG TTCTTCCATCTACACTGGCATTCTCTGAACCTCAGCCACCTTCTGGTTTTGC AGCTGGCTCAGTGTCTCTGTGTGAAGATTGCTACATCACACTCC ACCTTCTGTGTCTCAAGTCTAGACGCCAAGGGC</p>
<p>>mGR29 aa</p> <p>MDGIVQNMFTFIVIVEIIIGWIGNG FIALVNCIHWHYKRRKISALNQILTA LAFSRIYLLLTVFTVIAVSTLYTHV LVTRRVVKLINFHLLFSNHFMSWLA ACLGLEYFLKIAHFPNSIFVYLKMR INQVSGTLLMSLGLLFLNLTLLINS YIDTKIDDYREHLLYDFTSNNTASF YRVILVINNCIFTSIPFTLSQSTFL LLIFSLWRHYKKMQQHAQRCRDVLA DAHIRVLQTMVTVLLCAIFFLSLS MQILRSELLKNILYVRFCEIVAASF PSGHSCVLICRDTNLRGTFLSVLSW LKQRFTSWIPNINCRSSCIF</p>	<p>>mGR29 nt</p> <p>AGCTTGATATTTCTATTTGTTACTGCACAGAGTTTTTTTTTAAAAATTGAG TTTTTTATGTGATTCAATACTCAGATAGAGCTCTTTAATTTTTTACAGT GACCTCATGAATCATAACTTGCTTACAGACAATGGATGGAAATCGTACAGA ACATGTTTACATTCATTGTAATTGTGGAATAATAATAGGATGGATTGGAA ATGGATTCATAGCTCTGGTGAACCTGCATACACTGGTACAAGAGAAAGAA TCTCTGCACTGAATCAAATACTCACAGCCTTGGCTTTCTCCAGAATCTACC TTCTTTTAAACAGTATTCACGTGTATAGCAGTGTCTACGTATACACACACG TGTTGGTAAC TAGAAGAGTGGTAAACTGATTAATTTCCATTTGCTTTTCA GCAATCATTTAGCATCTGGCTTGCTGCATGCCTTGGCCTTTATTATTTTC TTAAATAGCTCATTTCCTAACTCTATTTTGTCTTAAAGATGAGAA TTAACCAGGTGGTTTCAGGACTTTGCTCATGTCTTTGGGCCTCTTGTTTC TAAACACTCTGCTGATAAACTCATACATGATACCAAGATAGATGACTACA GAGAACATCTACTGTATGATTTCACTTCGAATAATACTGCTTCATTTTACA GGGTATTTTATGCTATTAACTGATTTTTCACATCTATACCTTTACAC TTTCCAGTCCACTTTTCTCTGCTCATCTTCTCCCTGTGGAGACATTACA AGAAGATGCAACAGCATGCACAAAGATGCAGAGATGTCCTTGCAGATGCCC ACATCAGAGTCTTGCAAACCATGGTCACCTATGTCTACTCTGTGCCATTT TCTTTCTGTCTCTTCCATGCAAATTTTGAGGAGTGAAGTTGTTGAAGAACA TTCTTTACGTTAGGTTCTGCGAGATTGTTGCAGCAGTTTTCCTTCAGGAC ACTCCTGTGTCTTAATCTGTAGAGACACAAACCTGAGAGGACCTTTCTTT CTGTGCTATCGTGGCTGAAGCAGAGGTTTACATCATGGATTCTTAACATAA ATTGCAGATCATCTTGCATATTCTAAAGAAACTGAG</p>
<p>>mGR30 aa</p> <p>MTYETDITLMLVAVGEALVGILGNA FIALVNFMGWMKNRKIASIDLILSS VAMSRICLQCIILLDCIILVQYPTD YNRGKEMRTVDFFWTLTNHLSVWFA TCLSI FYLFKIANFFHPLFLWIKWR IDKLILRTLLACV IISLCFSLPVTE NLSDDFRRCVKTKERINSTLRCKVN KAGHASVKVNLNLVMLFPFSVSLVS FLLLILSLWRHTRQIQLSVTGYPKDP STTAHV KAMKAVISFLALFVYCLA FLIATSSYFMPESLAVIWGELIAL IYPSSH FILILGSSKLQASVRVL CRVKTMLKGKKY</p>	<p>>mGR30 nt</p> <p>AAAAATGTTTCATTGTTTATCTAAATTCAAATTTAACTGAGTGGCCTACAT TTTTATTTATTCAATCTAGTAGCTGTACTGAGGTTATTAGTGTGATTTCTG AAGCCCAAATTTGTAAACTTAGCCTCAGATAAACAGCTTGAGACCATGGA AAGTAATTTGGTAAA TTTGCATCTTAGCAAATAGTAGCTCAGCCTAAATTA ACTGTGTGTAGAAAAGAATGACCTGCGGAGAAGATAAATGGACATACAATA TCCAGGCTAAGGATTGCCAAACACACTGTTTTTAAGACTAATTGAGATTTA GATAAACTATCTACAGTCTTCATGTATAATTCTCATCTTCATCACAGACA GACTTCAACTTAAGGAGGTAAAGACAAGGACAGCGAACCTAAACAGCCAA GTGTAGAAACCAAACCTGCATCAAATCAGCCAGAACTAATTGGATACTTCT CTACTTTAAATGACATACGAAACAGATACTACCTTAATGCTTTGTAGCTGT TGGTGAAGCCTTAGTAGGGATTTTAGGAAATGCATTCATTGCCTGTTAA CTTCATGGGCTGGATGAAGAATAGGAAGATTGCCTCTATTGATTTAATCCT CTCAAGTGTGGCCATGTCCAGAATTTGTCTACAGTGTATAATCCTATTAGA TTGTATTATATTGGTGCAGTATCCAGACACCTACAACAGAGGTAAAGAAAT GAGGACCGTTGACTTCTTCTGGACACTTACCAACCATTAAAGTGTCTGGTT TGCCACCTGCCTCAGCATTTTCTATTTATTCAAGATAGCAAACCTCTTCCA CCCTCTTTTCTCTGGATAAAGTGGAGAATTGACAAGCTAATCTCAGAAC TCTACTGGCATGTGTGATTATCTCCCTGTGTTTTAGCCTCCAGTCACTGA AAATCTGAGTGTGATTTTCAGACGTTGTGTTAAGACAAAGGAGAGAATAAA CTCTACTTTGAGATGCAAAGTAAATAAGCTGGACATGCCTCTGTCAAGGT AAATCTCAACTTGGTCTGTCTGTTCCCTTTTCTGTCTCTCTGTCTCTCT TCTCCTCTTGATCCTCTCCCTGTGGAGACACACCAGGCAGATACAACCTCAG TGTAACAGGGTACAAAGATCCCAGCACACAGCTCATGTGAAGCCATGAA</p>

DECLARATION

As a below named inventor, I declare that:

My residence, post office address and citizenship are as stated below next to my name; I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **T2R, A NOVEL FAMILY OF TASTE RECEPTORS** the specification of which X is attached hereto or was filed on as Application No. and was amended on (if applicable).

I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56. I claim foreign priority benefits under Title 35, United States Code, Section 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)

Country	Application No.	Date of Filing	Priority Claimed Under 35 USC 119

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below:

Application No.	Filing Date

I claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

Application No.	Date of Filing	Status
09/393,634	09/10/99	Pending

Full Name of Inventor 1:	Last Name: ZUKER	First Name: CHARLES	Middle Name or Initial: S.	
Residence & Citizenship:	City: San Diego	State/Foreign Country: California	Country of Citizenship: United States	
Post Office Address:	Post Office Address: 4778 Thurston Place	City: San Diego	State/Country: California	Postal Code: 92130
Full Name of Inventor 2:	Last Name: ADLER	First Name: JON	Middle Name or Initial: Elliot	
Residence & Citizenship:	City: Washington	State/Foreign Country: D.C.	Country of Citizenship: United States	
Post Office Address:	Post Office Address: 1730 P. Street N.W.	City: Washington	State/Country: D.C.	Postal Code: 20036

Full Name of Inventor 3:	Last Name: RYBA	First Name: NICK	Middle Name or Initial:	
Residence & Citizenship:	City: Bethesda	State/Foreign Country: Maryland	Country of Citizenship: United Kingdom	
Post Office Address:	Post Office Address: 9202 Lundigen Court	City: Bethesda	State/Country: Maryland	Postal Code: 20817
Full Name of Inventor 4:	Last Name: MUELLER	First Name: KEN	Middle Name or Initial:	
Residence & Citizenship:	City: San Diego	State/Foreign Country: California	Country of Citizenship: United States	
Post Office Address:	Post Office Address: 9585 Genesee Ave., Apt. H1	City: San Diego	State/Country: California	Postal Code: 92121

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signature of Inventor 1 _____ CHARLES S. ZUKER Date	Signature of Inventor 2 _____ JON ELLIOT ADLER Date	Signature of Inventor 3 _____ NICK RYBA Date
Signature of Inventor 4 _____ KEN MUELLER Date		